

=> fil reg

FILE 'REGISTRY' ENTERED AT 10:37:20 ON 05 JUL 2005

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STRUCTURE FILE UPDATES: 4 JUL 2005 HIGHEST RN 853727-85-2

DICTIONARY FILE UPDATES: 4 JUL 2005 HIGHEST RN 853727-85-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

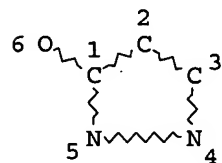
```
*****
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*
*****
```

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d sta que l34

```
L7          3 SEA FILE=REGISTRY ABB=ON  PLU=ON  (100-63-0/BI OR 141-97-9/BI
              OR 89-25-8/BI)
L8          1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L7 AND N2C3/ES
L9          21 SEA FILE=REGISTRY ABB=ON  PLU=ON  89-25-8/CRN
L10         STR
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#### NODE ATTRIBUTES:

CONNECT IS E2 RC AT 4

CONNECT IS E1 RC AT 6

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

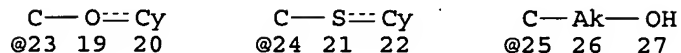
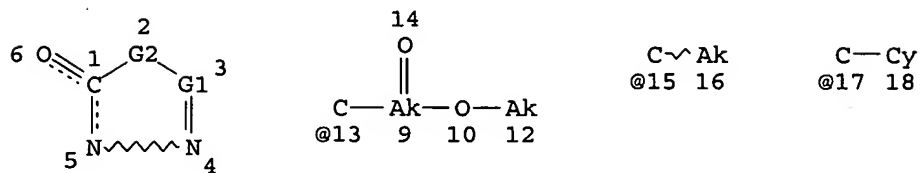
#### GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 6

STEREO ATTRIBUTES: NONE

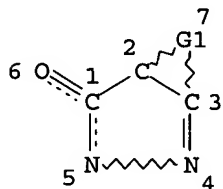
L12 93380 SEA FILE=REGISTRY SSS FUL L10  
L15 STR



VAR G1=C/13/15/17  
VAR G2=C/23/24/15/25  
NODE ATTRIBUTES:  
CONNECT IS M1 RC AT 5  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RSPEC 1  
NUMBER OF NODES IS 24

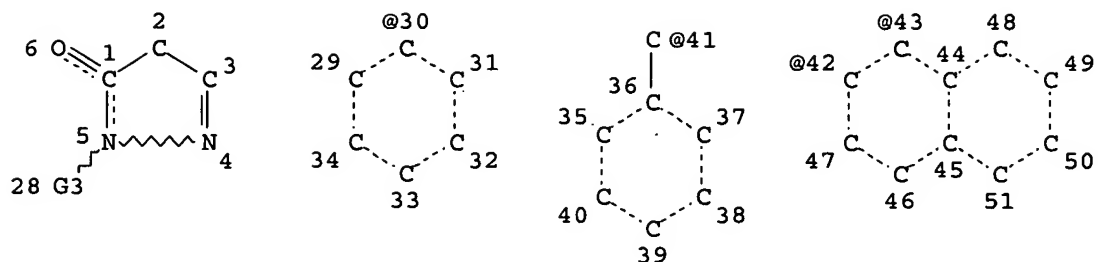
STEREO ATTRIBUTES: NONE  
L17 2711 SEA FILE=REGISTRY SUB=L12 CSS FUL L15  
L18 STR



REP G1=(1-3) C  
NODE ATTRIBUTES:  
CONNECT IS M1 RC AT 5  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RSPEC 1  
NUMBER OF NODES IS 7

STEREO ATTRIBUTES: NONE  
L20 6 SEA FILE=REGISTRY SUB=L12 CSS FUL L18  
L21 STR



Ak—OH  
@26 27

VAR G3=H/AK/CB/26/41/30/43/42

NODE ATTRIBUTES:

CONNECT IS M1 RC AT 2

CONNECT IS M1 RC AT 3

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

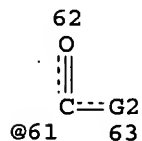
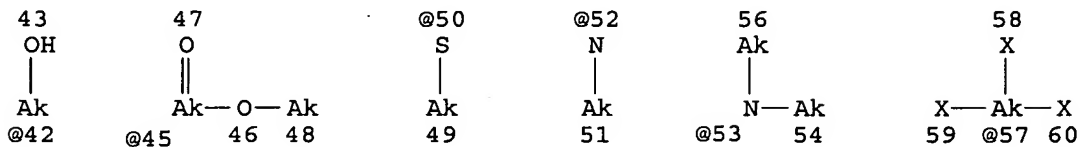
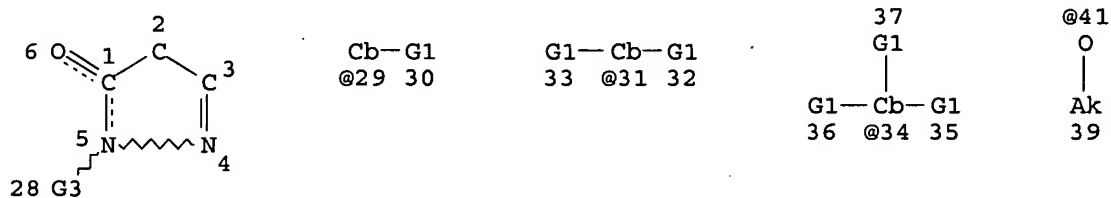
RSPEC 1 29 35 42

NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE

L23 472 SEA FILE=REGISTRY SUB=L17 CSS FUL L21

L24 STR



VAR G1=AK/41/42/45/50/52/53/57/61/X/CN/OH/NO2/NH2

VAR G2=OH/NH2

VAR G3=29/31/34

NODE ATTRIBUTES:

CONNECT IS M1 RC AT 2

CONNECT IS M1 RC AT 3

DEFAULT MLEVEL IS ATOM  
 GGCAT IS MCY UNS AT 29  
 GGCAT IS MCY UNS AT 31  
 GGCAT IS MCY UNS AT 34  
 DEFAULT ECLEVEL IS LIMITED  
 ECOUNT IS E6 C AT 29  
 ECOUNT IS E6 C AT 31  
 ECOUNT IS E6 C AT 34

## GRAPH ATTRIBUTES:

RSPEC 1  
 NUMBER OF NODES IS 38

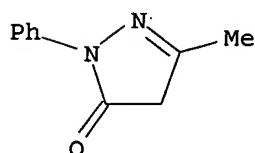
## STEREO ATTRIBUTES: NONE

L26 480 SEA FILE=REGISTRY SUB=L17 CSS FUL L24  
 L27 5 SEA FILE=REGISTRY ABB=ON PLU=ON L20 NOT 748176-18-3  
 L28 957 SEA FILE=REGISTRY ABB=ON PLU=ON (L23 OR L26 OR L27)  
 L29 935 SEA FILE=REGISTRY ABB=ON PLU=ON L28 NOT (L8 OR L9)  
 L30 909 SEA FILE=REGISTRY ABB=ON PLU=ON L29 NOT (MXS OR PMS OR  
 IDS)/CI  
 L31 44 SEA FILE=REGISTRY ABB=ON PLU=ON L30 AND NC>=2  
 L32 19 SEA FILE=REGISTRY ABB=ON PLU=ON L31 AND CLH AND 2/NC  
 L33 865 SEA FILE=REGISTRY ABB=ON PLU=ON L30 NOT L31  
 L34 884 SEA FILE=REGISTRY ABB=ON PLU=ON (L32 OR L33)

=> d ide can l8

L8 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN  
 RN 89-25-8 REGISTRY  
 ED Entered STN: 16 Nov 1984  
 CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 2-Pyrazolin-5-one, 3-methyl-1-phenyl- (8CI)  
 OTHER NAMES:  
 CN 1-Phenyl-3-methyl-2-pyrazolin-5-one  
 CN 1-Phenyl-3-methyl-5-oxopyrazole  
 CN 1-Phenyl-3-methyl-5-pyrazolinone  
 CN 1-Phenyl-3-methyl-5-pyrazolone  
 CN 2,4-Dihydro-5-methyl-2-phenyl-3H-pyrazol-3-one  
 CN 3-Methyl-1-phenyl-1H-pyrazol-5-one  
 CN 3-Methyl-1-phenyl-2-pyrazolin-5-one  
 CN 3-Methyl-1-phenyl-2-pyrazoline-5-one  
 CN 3-Methyl-1-phenyl-4,5-dihydropyrazol-5-one  
 CN 3-Methyl-1-phenyl-5-pyrazolone  
 CN 3-Methyl-1-phenylpyrazol-5(4H)-one  
 CN 3-Methyl-1-phenylpyrazolin-5-one  
 CN 5-Methyl-2-phenylpyrazol-3-one  
 CN C.I. Developer 1  
 CN Developer Z  
 CN Edarabone  
 CN Edaravone  
 CN MCI 186  
 CN Methylphenylpyrazolone  
 CN NCI-C 03952  
 CN Norantipyrene  
 CN Norphenazone  
 CN NSC 12  
 CN NSC 26139  
 CN NSC 2629

CN Radicut  
FS 3D CONCORD  
DR 12235-58-4, 62495-97-0, 115566-83-1, 72134-66-8, 52224-17-6, 206195-95-1  
MF C10 H10 N2 O  
CI COM  
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN\*,  
BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT,  
CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHM, DDFU, DRUGU,  
EMBASE, GMELIN\*, HODOC\*, HSDB\*, IFICDB, IFIPAT, IFIUDB, IMSDRUGNEWS,  
IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK\*, MSDS-OHS, NIOSHTIC, PHAR,  
PIRA, PROMT, PROUSDDR, PS, RTECS\*, SPECINFO, SYNTHLINE, TOXCENTER, USAN,  
USPAT2, USPATFULL, VETU  
(\*File contains numerically searchable property data)  
Other Sources: DSL\*\*, EINECS\*\*, TSCA\*\*, WHO  
(\*\*Enter CHEMLIST File for up-to-date regulatory information)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2225 REFERENCES IN FILE CA (1907 TO DATE)  
65 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
2230 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
16 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 143:31877  
REFERENCE 2: 143:19725  
REFERENCE 3: 143:1170  
REFERENCE 4: 142:487534  
REFERENCE 5: 142:472654  
REFERENCE 6: 142:470231  
REFERENCE 7: 142:451447  
REFERENCE 8: 142:443911  
REFERENCE 9: 142:441766  
REFERENCE 10: 142:441672

=> d his

(FILE 'HOME' ENTERED AT 09:38:26 ON 05 JUL 2005)  
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 09:38:42 ON 05 JUL 2005

jan delaval - 5 july 2005

L1 1 S US20040254234/PN OR (US2003-643404# OR JP2002-258503)/AP,PRN  
E TANAKA T/AU  
L2 1839 S E3-E9,E103  
E TAKAYUKI/AU  
L3 2 S E3  
E MORI T/AU  
L4 1572 S E3-E7  
E MORI TATSU/AU  
L5 15 S E7,E8  
E TATSUHIKO M/AU  
E MITSUBISHI/PA,CS  
L6 136872 S MITSUBISHI/PA,CS  
SEL RN L1

FILE 'REGISTRY' ENTERED AT 09:41:24 ON 05 JUL 2005

L7 3 S E1-E3  
L8 1 S L7 AND N2C3/ES  
L9 21 S 89-25-8/CRN  
L10 STR  
L11 50 S L10  
L12 93380 S L10 FUL  
L13 STR L10  
L14 50 S L13 CSS SAM SUB=L12  
L15 STR L13  
L16 39 S L15 CSS SAM SUB=L12  
L17 2711 S L15 CSS FUL SUB=L12  
SAV L17 KWON643/A  
L18 STR L15  
L19 0 S L18 CSS SAM SUB=L12  
L20 6 S L18 CSS FUL SUB=L12  
SAV L20 KWON643A/A  
L21 STR L15  
L22 22 S L21 CSS SAM SUB=L17  
L23 472 S L21 CSS FUL SUB=L17  
SAV L23 KWON643B/A  
L24 STR L21  
L25 27 S L24 CSS SAM SUB=L17  
L26 480 S L24 CSS FUL SUB=L17  
SAV L26 KWON643C/A  
L27 5 S L20 NOT 748176-18-3  
L28 957 S L23,L26,L27  
SAV L28 KWON643D/A  
L29 935 S L28 NOT L8,L9  
L30 909 S L29 NOT (MXS OR PMS OR IDS)/CI  
L31 44 S L30 AND NC>=2  
L32 19 S L31 AND CLH AND 2/NC  
L33 865 S L30 NOT L31  
L34 884 S L32,L33

FILE 'HCAPLUS' ENTERED AT 10:05:39 ON 05 JUL 2005

L35 2230 S L8  
L36 12 S L9  
L37 2 S L36 AND (PHARMACEUT? OR PHARMACOL?)/SC,SX  
L38 113 S EDARA!ON#  
L39 86 S 1 PHENYL 3 METHYLPYRAZOL 5 ONE  
L40 451 S 3 METHYL 1 PHENYL 2 PYRAZOLIN 5 ONE  
L41 1585 S 1 PHENYL 3 METHYL 5 PYRAZOLONE  
L42 552 S 3 METHYL 1 PHENYL 5 PYRAZOLONE  
L43 138 S 1 PHENYL 3 METHYLPYRAZOLONE  
L44 46 S 2 4 DIHYDRO 5 METHYL 2 PHENYL 3H PYRAZOL 3 ONE

L45 71 S MCI186 OR MCI 186  
 L46 177 S NORANTIPYRIN?  
 L47 36 S 3 METHYL 1 PHENYL 2 PYRAZOLINE 5 ONE  
 L48 21 S 1 PHENYL 3 METHYL 5 PYRAZOLINONE  
 L49 54 S 3 METHYL 1 PHENYLPYRAZOL 5 ONE  
 L50 2 S 3 METHYL 1 PHENYL 4 5 DIHYDROPYRAZOL 5 ONE  
 L51 4070 S L35-L50  
 L52 2338 S L34  
 L53 5809 S L51,L52  
 L54 114 S L53 AND L1-L6  
 L55 253 S ARTERIAL (L) WALL (L) FAIL?  
 L56 749 S ARTERIAL (L) WALL (L) INJUR?  
 L57 375 S ARTERIAL (L) WALL (L) DAMAG?  
 L58 1 S L53 AND L55-L57  
 E ARTERY, DISEASE/CT  
 E E3+ALL  
 L59 21055 S E7+OLD  
 L60 58106 S E7+NT  
 L61 76585 S E7+RT  
 E E54+ALL  
 L62 80239 S E5+OLD,NT  
 L63 23 S L53 AND L59-L62  
 L64 23 S L58,L63  
 L65 897 S PERCUTAN? (L) TRANSLUMIN? (L) (HEART OR MYOCARD? OR CORON?) (L) ANG  
 L66 913 S PTCA  
 L67 1193 S CORONAR? (L) ARTER? (L) BYPASS? (L) ?GRAFT?  
 L68 12 S CORONAR? (L) ARTER? (L) BY PASS? (L) ?GRAFT?  
 L69 472 S CABG  
 L70 1 S L53 AND L65-L69  
 E RESTENOSIS/CT  
 E E3+ALL  
 L71 4523 S E2,E3  
 L72 6548 S RESTENOS?  
 L73 2544 S NEOINTIM?  
 L74 3 S L53 AND L71-L73  
 L75 23 S L64,L70,L74  
 E BYPASS/CT  
 E CORONARY BYPASS/CT  
 L76 1 S E23  
 E ARTERIAL BYPASS/CT  
 L77 0 S L53 AND L76  
 L78 2 S L75 AND L54  
 L79 21 S L75 NOT L78  
 L80 11 S L79 AND (PD<=20020904 OR PRD<=20020904 OR AD<=20020904)  
 SEL DN AN 2 3 4 6 8  
 L81 5 S L80 AND E1-E15  
 L82 6 S L80 NOT L81  
 SEL DN AN 1 5  
 L83 2 S L82 AND E16-E21  
 L84 9 S L78,L81,L83  
 L85 9 S L84 AND L1-L6,L35-L84

FILE 'REGISTRY' ENTERED AT 10:37:20 ON 05 JUL 2005

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 10:37:53 ON 05 JUL 2005

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FILE COVERS 1907 - 5 Jul 2005 VOL 143 ISS 2  
FILE LAST UPDATED: 4 Jul 2005 (20050704/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l85 all hitstr tot

L85 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN  
AN 2005:545579 HCAPLUS  
ED Entered STN: 24 Jun 2005  
TI Pyrazolones and arginine amide derivatives for prevention and treatment of intra carotid artery occlusion and stenosis  
IN Takahashi, Hiroshi; Sato, Akihiko; Yamamoto, Toshiki  
PA Mitsubishi Welpharma Co., Japan  
SO Jpn. Kokai Tokkyo Koho, 14 pp.  
CODEN: JKXXAF  
DT Patent  
LA Japanese  
IC ICM A61K031-4152  
ICS A61K031-4709; A61P009-10  
CC 1-8 (Pharmacology)  
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2005162749	A2	20050623	JP 2004-331133	20041115
PRAI JP 2003-384704	A	20031114		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
JP 2005162749	ICM	A61K031-4152
	ICS	A61K031-4709; A61P009-10
JP 2005162749	FTERM	4C086/AA01; 4C086/AA02; 4C086/BC28; 4C086/BC36; 4C086/GA07; 4C086/MA02; 4C086/MA04; 4C086/ZA36; 4C086/ZA39

AB Pyrazolones (I; R1, R2 = H, aryl, alkyl, etc.; R3 = H, alkyl, cycloalkyl. etc.) and arginine amide derivs. (II; R4 = alkylcarboxypiperidino; R5 = Ph, low alkyl, etc.) and their physiol acceptable salts and hydrates are claimed for prevention and treatment of intra carotid artery occlusion and stenosis.

ST pyrazolone arginine amide deriv carotid artery occlusion stenosis

IT INDEXING IN PROGRESS

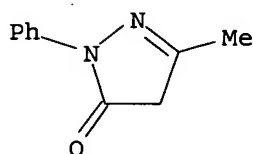
IT Artery, disease  
(carotid, occlusion; pyrazolones and arginine amide derivs. for prevention and treatment of intra carotid artery occlusion and stenosis)

IT Artery, disease



(carotid, **stenosis**; pyrazolones and arginine amide derivs.  
for prevention and treatment of intra carotid artery **occlusion**  
and **stenosis**)

IT Human  
(pyrazolones and arginine amide derivs. for prevention and treatment of  
intra carotid artery occlusion and stenosis)  
IT 74-79-3D, L-Arginine, amide derivs. and salts 89-25-8, 3  
-Methyl-1-phenyl-2-  
pyrazolin-5-one 39455-90-8D, Pyrazolone,  
derivs. and salts  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(pyrazolones and arginine amide derivs. for prevention and treatment of  
intra carotid artery occlusion and stenosis)  
IT INDEXING IN PROGRESS  
IT 89-25-8, 3-Methyl-1-phenyl  
-2-pyrazolin-5-one  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(pyrazolones and arginine amide derivs. for prevention and treatment of  
intra carotid artery occlusion and stenosis)  
RN 89-25-8 HCAPLUS  
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (9CI) (CA INDEX NAME)



L85 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN  
AN 2004:310105 HCAPLUS  
DN 140:297521  
ED Entered STN: 16 Apr 2004  
TI Pyrazolone derivatives for treatment and/or prevention of **arterial**  
**wall failure**  
IN Tanaka, Takayuki; Mori, Tatsuhiko  
PA Mitsubishi Welfharma Co., Japan  
SO Jpn. Kokai Tokkyo Koho, 12 pp.  
CODEN: JKXXAF  
DT Patent  
LA Japanese  
IC ICM A61K031-4152  
ICS A61P009-10; C07D231-22  
CC 1-8 (Pharmacology)  
Section cross-reference(s): 63

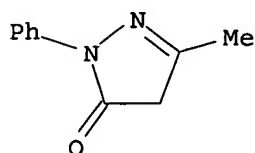
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2004115505	A2	20040415	JP 2003-311057	20030903 <--
	US 2004254234	A1	20041216	US 2003-643404	20030818 <--
PRAI	JP 2002-258503	A	20020904	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
JP 2004115505	ICM	A61K031-4152

ICS A61P009-10; C07D231-22  
JP 2004115505 FTERM 4C086/AA01; 4C086/AA02; 4C086/BC36; 4C086/HA24;  
4C086/MA01; 4C086/NA14; 4C086/ZA45 <--  
US 2004254234 NCL 514/404.000 <--  
OS MARPAT 140:297521  
AB The invention provides pyrazolone derivs., e.g. 3-methyl  
-1-phenyl-2-pyrazolin-5-  
one (Edaravone) for treatment and/or prevention of  
arterial wall failure, e.g. coronary  
restenosis after percutaneous transluminal  
coronary angioplasty (PTCA) and  
coronary artery bypass graft (  
CABG) surgery. The effect of Edaravone on  
arterial neo-intima in rabbits fed a high-cholesterol diet was  
examined  
ST pyrazolone deriv arterial wall failure  
treatment; Edaravone arterial restenosis  
treatment  
IT Artery, disease  
(coronary, restenosis; pyrazolone derivs. for  
treatment and/or prevention of arterial wall  
failure)  
IT Artery, disease  
(pyrazolone derivs. for treatment and/or prevention of arterial  
wall failure)  
IT 100-63-0, Phenylhydrazine 141-97-9, Ethyl acetoacetate  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of pyrazolone derivs. for treatment and/or prevention of  
arterial wall failure)  
IT 89-25-8P, Edaravone  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)  
(pyrazolone derivs. for treatment and/or prevention of arterial  
wall failure)  
IT 89-25-8P, Edaravone  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)  
(pyrazolone derivs. for treatment and/or prevention of arterial  
wall failure)  
RN 89-25-8 HCAPLUS  
CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (9CI) (CA INDEX NAME)



L85 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN  
AN 2004:101148 HCAPLUS  
DN 140:163867  
ED Entered STN: 08 Feb 2004  
TI Preparation of indane, dihydrobenzofuran and tetrahydronaphthalene  
carboxylic acid derivatives as antidiabetic agents

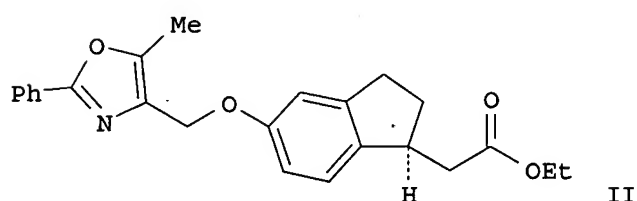
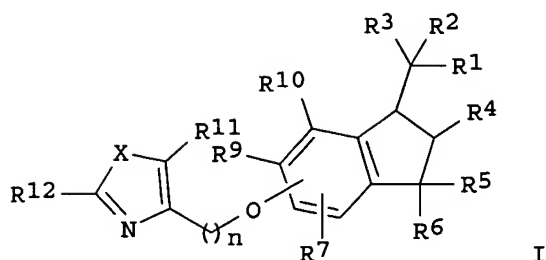
IN Wickens, Philip; Cantin, Louis-David; Chuang, Chih-Yuan; Dai, Miao;  
Hentemann, Martin F.; Kumarasinghe, Ellalahewage; Liang, Sidney X.; Lowe,  
Derek B.; Shelekhin, Tatiana E.; Wang, Yamin; Zhang, Chengzhi; Zhang,  
Hai-Jun; Zhao, Qian  
PA Bayer Pharmaceuticals Corporation, USA  
SO PCT Int. Appl., 204 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
IC ICM C07D263-32  
ICS C07D277-26; C07D277-40; C07D277-48; C07D277-52; C07D233-68;  
C07D233-64; C07D405-10; C07D401-10; C07D413-10; C07D231-12;  
C07D231-20; C07D231-16; C07D413-12; A61K031-431  
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1, 63

## FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004011446	A1	20040205	WO 2003-US23342	20030725 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI US 2002-399095P	P	20020726 <--		

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004011446	ICM	C07D263-32
	ICS	C07D277-26; C07D277-40; C07D277-48; C07D277-52; C07D233-68; C07D233-64; C07D405-10; C07D401-10; C07D413-10; C07D231-12; C07D231-20; C07D231-16; C07D413-12; A61K031-431
WO 2004011446	ECLA	C07D231/12B5; C07D231/16; C07D231/20; C07D233/54C3; C07D263/32; C07D277/40; C07D277/46; C07D277/48; C07D277/52; C07D413/04+263B+213; C07D413/12+307+263B; C07D413/12+317+263B; C07D417/12+307+277B; C07D233/68<--
OS	MARPAT 140:163867	
GI		



- AB Title compds., e.g., I [X = O, S; n = 1-3; R1 = carboxy, carboxamide, alkylamino, etc.; R2-3 = H, F, alkyl; R4-6 = H, alkyl; R7 = H, alkoxy, OH, etc.; R9 = H, Br, Cl, I, alkyl, etc.; R10 = H, OSO<sub>2</sub>CF<sub>3</sub>, etc.; R11 = H, alkyl, etc.; R12 = naphthyl, pyridyl, etc.] are prepared For instance, Et (S)-[5-hydroxy-2,3-dihydro-1H-inden-1-yl]acetate (preparation given) is coupled to 4-chloromethyl-5-methyl-2-phenyloxazole (preparation given; DMF, K<sub>2</sub>CO<sub>3</sub>, 3 h, 80°) to give II. I are useful in the treatment of diseases such as diabetes, diabetes-related disorders, obesity, hyperlipidemia and cardiovascular diseases.
- ST indane dihydrobenzofuran tetrahydronaphthalene carboxylate deriv  
antidiabetic prepn
- IT Adrenoceptors  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(agonists, combination pharmaceutical; preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)
- IT Heart, disease  
(angina pectoris; preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)
- IT Ischemia  
(cardiac; preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)
- IT Antidiabetic agents  
Antihypertensives  
(combination pharmaceutical; preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)
- IT Sulfonylureas  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(combination pharmaceutical; preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)
- IT Artery, disease  
(coronary; preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)

- IT Lipids, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(dyslipidemia; preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)
- IT Pregnancy  
(gestational diabetes mellitus; preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)
- IT Diabetes mellitus  
(gestational; preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)
- IT Lipoproteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(high-d.; preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)
- IT Heart, disease  
(infarction; preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)
- IT Heart, disease  
(ischemia; preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)
- IT Disease, animal  
(metabolic syndrome X; preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)
- IT Antianginal agents  
Antiobesity agents  
Cardiovascular agents  
Diabetes insipidus  
Diabetes mellitus  
Heart, disease  
Human  
Hypercholesterolemia  
Hyperglycemia  
Hypertension  
Hypertriglyceridemia  
Obesity  
Pheochromocytoma  
(preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)
- IT Bile acids  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(sequestrant, combination pharmaceutical; preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)
- IT Brain, disease  
(stroke; preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)
- IT 9004-10-8D, Insulin, sensitizers, secretagogues  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(combination pharmaceutical; preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)
- IT 59-67-6, Nicotinic acid, biological studies 943-45-3D, Fibric acid, derivs.  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(combination pharmaceutical; preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)
- IT 9001-62-1, Lipase 9028-35-7, HMG-CoA reductase 74315-95-0,  $\alpha$ -Glycosidase  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)  
(inhibitor, combination pharmaceutical; preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)

IT 9004-10-8, Insulin, biological studies

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)

IT 652980-38-6P, Ethyl (S)-[5-[(5-methyl-2-phenyl-1,3-oxazol-4-yl)methoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652980-41-1P, Ethyl (S)-[6-[3-(5-methyl-2-phenyl-1,3-oxazol-4-yl)propoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652980-43-3P 652980-51-3P, Ethyl difluoro[5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652980-74-0P 652980-93-3P 652981-05-0P, Ethyl [7-(3-chloro-4-fluorophenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652981-82-3P, Ethyl (S)-[5-[2-(2-iodo-5-methyl-1H-imidazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652981-86-7P, Ethyl (S)-[5-[2-[2-(2,4-dimethylphenyl)-5-methyl-1H-imidazol-4-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652981-94-7P, Ethyl (S)-[6-[2-(1,4-dimethyl-2-phenyl-1H-imidazol-5-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652982-16-6P, Ethyl (S)-[5-[(2-bromo-1-pentyl-1H-imidazol-5-yl)methoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652982-23-5P, Ethyl (S)-[5-[2-[2-(4-bromophenyl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652982-28-0P, Methyl (2S)-2-[(1S)-5-[2-[2-(4-bromophenyl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoate 652982-29-1P, Methyl (2S)-2-[(1S)-5-[2-[2-(3',4'-dimethyl-1,1'-biphenyl-4-yl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoate 652982-34-8P, (S)-[5-[2-[2-[4-(Benzylamino)phenyl]-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-39-3P, (S)-[5-[2-[2-(4-Allylphenyl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-73-5P 652982-94-0P, Ethyl (S)-[5-[2-(4-bromo-3,5-dimethyl-1H-pyrazol-1-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652982-95-1P, Ethyl (S)-[5-[2-[4-(4-tert-butylphenyl)-3,5-dimethyl-1H-pyrazol-1-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)

IT 652980-39-7P, (S)-[5-[(5-Methyl-2-phenyl-1,3-oxazol-4-yl)methoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652980-40-0P 652980-42-2P, (S)-[6-[3-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)propoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652980-45-5P, (S)-N,N-Dimethyl-2-[5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]ethanamine 652980-46-6P, (S)-2-[5-[2-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]ethanamine 652980-47-7P 652980-48-8P 652980-49-9P, (S)-N-Methyl-2-[5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]ethanamine 652980-56-8P, Difluoro[5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652980-57-9P, rel-Methyl (2S)-2-[(1S)-3,3-dimethyl-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-indene-1-yl]butanoate 652980-64-8P, rel-(2S)-2-[(1S)-3,3-Dimethyl-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-indene-1-yl]butanoic acid 652980-65-9P, [3,3-Dimethyl-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652980-67-1P, (S)-[5-[2-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-6-(phenylethynyl)-2,3-dihydro-1H-inden-1-yl]acetic acid 652980-71-7P, (S)-[6-Allyl-5-[2-(5-

methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652980-72-8P, Ethyl (S)-[5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-6-(2-phenylethyl)-2,3-dihydro-1H-inden-1-yl]acetate 652980-73-9P, (S)-[5-[2-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-6-(2-phenylethyl)-2,3-dihydro-1H-inden-1-yl]acetic acid 652980-75-1P 652980-76-2P, [4-[2-[5-Methyl-2-(2-naphthyl)-1,3-oxazol-4-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652980-77-3P, [4-[2-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652980-78-4P, [4-[2-[2-(4-Fluorophenyl)-5-methyl-1,3-oxazol-4-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652980-79-5P, [4-[2-[2-(4-Fluoro-3-methylphenyl)-5-methyl-1,3-oxazol-4-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652980-80-8P, [2-Methyl-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652980-94-4P, [4-Methoxy-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652980-95-5P, [4-Hydroxy-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652980-96-6P, [4-(1,3-Benzodioxol-5-yl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652980-97-7P, [4-(4-Isopropylphenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652980-98-8P, [4-(4-Methoxyphenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-06-1P, [7-(3-Chloro-4-fluorophenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-07-2P, [7-(4-Methylphenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-08-3P, [7-(4-Fluorophenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-09-4P, [7-(4-Ethoxyphenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-10-7P, [7-(4-Chlorophenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-11-8P, [7-(4-Methoxyphenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-12-9P, [5-[2-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-7-[4-(methylsulfanyl)phenyl]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-13-0P, [7-(2-Methylphenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-14-1P, [7-(3-Methylphenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-15-2P, [7-(2,4-Dichlorophenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-16-3P, [7-(1,3-Benzodioxol-5-yl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-17-4P, [7-(4-Isopropylphenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-18-5P, [7-(3,4-Dimethylphenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-19-6P, [7-(3-Methoxyphenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-20-9P, [5-[2-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-7-[3-(trifluoromethyl)phenyl]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-21-0P, [7-(2-Methoxyphenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-22-1P, [5-[2-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-7-[2-(trifluoromethyl)phenyl]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-23-2P, [7-(2,4-Difluorophenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-24-3P, [7-(4-tert-Butylphenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-25-4P, [7-(4-Fluoro-3-methylphenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-26-5P, [7-(4-Ethylphenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-27-6P, [5-[2-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-7-

phenyl-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-28-7P  
 652981-33-4P, (S) - [5- [2- (5-Phenethyl-2-phenyloxazol-4-yl) ethoxy] indan-1-yl]acetic acid 652981-34-5P, (S) - [5- [2- [2- (4-Chlorophenyl) -5- [2- (4-methoxyphenyl) ethyl] oxazol-4-yl] ethoxy] indan-1-yl]acetic acid  
 652981-35-6P, (S) - [5- [2- [2- (4-Chlorophenyl) -5- [2- (2,6-dichlorophenyl) ethyl] oxazol-4-yl] ethoxy] indan-1-yl]acetic acid  
 652981-36-7P, (S) - [5- [2- [2- (4-Chlorophenyl) -5- (2-m-tolyethyl) oxazol-4-yl] ethoxy] indan-1-yl]acetic acid 652981-37-8P, (S) - [5- [2- [2- (4-Chlorophenyl) -5- (2-p-tolyethyl) oxazol-4-yl] ethoxy] indan-1-yl]acetic acid  
 652981-38-9P, (S) - [5- [2- [2- (4-Chlorophenyl) -5- [2- (4-chlorophenyl) ethyl] oxazol-4-yl] ethoxy] indan-1-yl]acetic acid  
 652981-39-0P, (S) - [5- [2- [5-Methyl-2- (6-phenyl-3-pyridinyl) -1,3-oxazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid 652981-42-5P, (2S) -2- [(1S) -5- [2- [5-Methyl-2- (6-phenyl-3-pyridinyl) -1,3-oxazol-4-yl] ethoxy] -2,3-dihydro-1H-indene-1-yl]propanoic acid 652981-47-0P, (S) - [5- [2- [2- [(Cyclohexylcarbonyl) amino] -5-methyl-1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid 652981-49-2P, (S) - [5- [2- (2-Amino-5-methyl-1,3-thiazol-4-yl) ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid  
 trifluoroacetate 652981-50-5P; Ethyl (S) - [5- [2- [2- [(anilinoacetyl) amino] -5-methyl-1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetate 652981-51-6P, (S) - [5- [2- [2- [(Anilinoacetyl) amino] -5-methyl-1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid  
 652981-52-7P, (S) - [5- [2- [5-Methyl-2- [(phenylsulfonyl) amino] -1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid 652981-53-8P, (S) - [5- [2- [5-Methyl-2- [(methylsulfonyl) amino] -1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid 652981-54-9P, (S) - [5- [2- [2- [(4-Methoxybenzoyl) amino] -5-methylthiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid 652981-55-0P, (S) - [5- [2- [2- (Benzoylamino) -5-methyl-1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid 652981-56-1P, (S) - [5- [2- [2- [(4-Fluorobenzoyl) amino] -5-methyl-1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid 652981-57-2P, (S) - [5- [2- [2- (Acetylamino) -5-methyl-1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid 652981-58-3P, (S) - [5- [2- [2- [(Cyclobutylcarbonyl) amino] -5-methyl-1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid  
 652981-59-4P, (S) - [5- [2- [2- [(1,1'-Biphenyl-4-yl) carbonyl] amino] -5-methylthiazol-4-yl] ethoxy] -2,3-dihydro-1H-indene-1-yl]acetic acid  
 652981-60-7P, (S) - [5- [2- [2- [(2-Methoxybenzoyl) amino] -5-methyl-1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid 652981-61-8P, (S) - [5- [2- [2- [(4-Chlorobenzoyl) amino] -5-methyl-1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid 652981-62-9P, (S) - [5- [2- [2- [(3,4-Dichlorobenzoyl) amino] -5-methyl-1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid 652981-63-0P, (S) - [5- [2- [2- [(3-Methoxybenzoyl) amino] -5-methyl-1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid 652981-64-1P, (S) - [5- [2- [5-Methyl-2- (((naphthalen-1-yl) carbonyl) amino) -1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid 652981-65-2P, (S) - [5- [2- [5-Methyl-2- [(3-methylbenzoyl) amino] -1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid 652981-66-3P, (S) - [5- [2- [5-Methyl-2- [(4-methylbenzoyl) amino] -1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid 652981-67-4P, (S) - [5- [2- [5-Methyl-2- [(4-nitrobenzoyl) amino] -1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid 652981-68-5P, (S) - [5- [2- [5-Methyl-2- [(3-nitrobenzoyl) amino] -1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid 652981-69-6P, (S) - [5- [2- [5-Methyl-2- [(2-nitrobenzoyl) amino] -1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid 652981-70-9P, (S) - [5- [2- [2- [(3-Chlorobenzoyl) amino] -5-methyl-1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid  
 652981-71-0P, (S) - [5- [2- [2- [(2-Chlorobenzoyl) amino] -5-methyl-1,3-thiazol-4-yl] ethoxy] -2,3-dihydro-1H-inden-1-yl]acetic acid 652981-72-1P, (S) - [5- [2- [2- [(2-Fluorobenzoyl) amino] -5-methyl-1,3-thiazol-4-yl] ethoxy] -



2,3-dihydro-1H-inden-1-yl]acetic acid 652981-73-2P, (S)-[5-[2-[5-Methyl-2-[(2-methylbenzoyl)amino]-1,3-thiazol-4-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-74-3P, (S)-[5-[2-[5-Methyl-2-[[[(4-methylphenyl)amino]carbonyl]amino]-1,3-thiazol-4-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-75-4P, (S)-[5-[2-[2-[[[(4-Fluorophenyl)amino]carbonyl]amino]-5-methyl-1,3-thiazol-4-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-76-5P, [4-[2-[2-(4-Fluorophenyl)-5-methyl-1,3-thiazol-4-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-84-5P, Ethyl (S)-[5-[2-[2-(4-methoxyphenyl)-4-methyl-1-pentyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652981-85-6P, Ethyl (S)-[5-[2-(2-iodo-5-methyl-1-pentyl-1H-imidazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652981-87-8P, (S)-[5-[2-[2-(2,4-Dimethylphenyl)-5-methyl-1H-imidazol-4-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-95-8P, (S)-[6-[2-(1,4-Dimethyl-2-phenyl-1H-imidazol-5-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-96-9P, [5-[2-[5-Methyl-2-(4-methoxyphenyl)-1-pentyl-1H-imidazol-4-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-97-0P, [5-[2-[2-(4-Methoxyphenyl)-4-methyl-1-pentyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-98-1P, (S)-[5-[2-(1-Benzyl-5-methyl-2-phenyl-1H-imidazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652981-99-2P, (S)-[5-[2-(1-Benzyl-4-methyl-2-phenyl-1H-imidazol-5-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-00-8P, (S)-[5-[2-[1-Benzyl-5-methyl-2-[4-(methylsulfanyl)phenyl]-1H-imidazol-4-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-01-9P, (S)-[5-[2-[1-Benzyl-2-(3-nitrophenyl)-5-methyl-1H-imidazol-4-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-02-0P, Ethyl (S)-[5-[2-[2-(4-methoxyphenyl)-5-methyl-1H-imidazol-4-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652982-03-1P, (S)-[5-[2-[5-Methyl-2-(4-methylphenyl)-1-pentyl-1H-imidazol-4-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-04-2P, (S)-[5-[2-[2-(4-Methoxyphenyl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-05-3P, (S)-[5-[2-[2-(1,1'-Biphenyl-4-yl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-06-4P, (S)-[5-[2-[2-(4-Ethylphenyl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-07-5P, Ethyl (S)-[5-[2-[2-(1,1'-biphenyl-4-yl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652982-09-7P, Ethyl (S)-[5-[2-[2-(4-ethylphenyl)-1,5-dimethyl-1H-imidazol-4-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652982-10-0P, (S)-[5-[2-(1,5-Dimethyl-2-phenyl-1H-imidazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-11-1P, (S)-[5-[2-[2-(4-Ethylphenyl)-1,5-dimethyl-1H-imidazol-4-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-12-2P, (S)-[5-[2-[2-(1,1'-Biphenyl-4-yl)-1,5-dimethyl-1H-imidazol-4-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-13-3P, (S)-[5-[2-[2-(4-Methoxyphenyl)-1,5-dimethyl-1H-imidazol-4-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-17-7P, (S)-[5-[(1-Pentyl-2-phenyl-1H-imidazol-5-yl)methoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-18-8P, (S)-[5-[[2-(4-Methoxyphenyl)-1-pentyl-1H-imidazol-5-yl]methoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-19-9P, (S)-[5-[[1-Pentyl-2-[4-(trifluoromethyl)phenyl]-1H-imidazol-5-yl]methoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-20-2P, (S)-[5-[[2-(1,3-Benzodioxol-5-yl)-1-pentyl-1H-imidazol-5-yl]methoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-21-3P, (S)-[5-[[2-(3,4-Dimethylphenyl)-1-pentyl-1H-imidazol-5-yl]methoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-22-4P, (S)-[5-[[1-Pentyl-2-(4-pyridinyl)-1H-imidazol-5-yl]methoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-30-4P, (2S)-2-[(1S)-5-[2-[2-(3',4'-Dimethyl-1,1'-biphenyl-4-yl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-31-5P, (S)-[5-[2-[1,4-Dimethyl-2-(4-methylphenyl)-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-32-6P, (2S)-2-[(1S)-5-[2-[2-(3'-Methoxy-1,1'-

biphenyl-3-yl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-33-7P, Ethyl (S)-[5-[2-[2-[4-(benzylamino)phenyl]-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652982-35-9P, (S)-[5-[2-[2-(4-Aminophenyl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-36-0P, Ethyl (S)-[5-[2-[2-(4-vinylphenyl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652982-37-1P, (S)-[5-[2-[2-(4-Vinylphenyl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-38-2P, Ethyl (S)-[5-[2-[2-(4-allylphenyl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652982-40-6P, (S)-[5-[2-[2-(4-Propylphenyl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-42-8P, (2S)-2-[(1S)-5-[2-[2-(1,1'-Biphenyl-4-yl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid trifluoroacetate 652982-44-0P, (2S)-2-[(1S)-5-[2-[2-(4-Ethylphenyl)-1,5-dimethyl-1H-imidazol-4-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid trifluoroacetate 652982-46-2P, (2S)-2-[(1S)-5-[2-[2-(4-Ethylphenyl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid trifluoroacetate 652982-47-3P, (S)-[5-[2-[2-(4-Bromophenyl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-48-4P, (S)-[5-[2-[1,4-Dimethyl-2-[4-(1H-pyrrol-2-yl)phenyl]-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-49-5P, (2S)-2-[(1S)-5-[2-[2-(4-Bromophenyl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-50-8P, (2S)-2-[(1S)-5-[2-[1,4-Dimethyl-2-phenyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-51-9P, (2S)-2-[(1S)-5-[2-[2-(4-Allylphenyl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-52-0P, (2S)-2-[(1S)-5-[2-[2-(4-Butylphenyl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-53-1P, (2S)-2-[(1S)-5-[2-[1,4-Dimethyl-2-(4-methylphenyl)-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-54-2P, (2S)-2-[(1S)-5-[2-[2-(4'-Methoxy-1,1'-biphenyl-4-yl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-55-3P, (2S)-2-[(1S)-5-[2-[2-[4-(1,3-Benzodioxol-5-yl)phenyl]-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-56-4P, (2S)-2-[(1S)-5-[2-[2-(4'-Fluoro-1,1'-biphenyl-4-yl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-57-5P, (2S)-2-[(1S)-5-[2-[1,4-Dimethyl-2-(3'-methyl-1,1'-biphenyl-4-yl)-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-58-6P, (2S)-2-[(1S)-5-[2-[1,4-Dimethyl-2-(4'-methyl-1,1'-biphenyl-4-yl)-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-59-7P, (2S)-2-[(1S)-5-[2-[2-(4'-Fluoro-3'-methyl-1,1'-biphenyl-4-yl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-60-0P, (2S)-2-[(1S)-5-[2-[2-[4-(2,4-Dihydroxy-5-pyrimidinyl)phenyl]-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-61-1P, (2S)-2-[(1S)-5-[2-[2-(4'-Ethyl-1,1'-biphenyl-4-yl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-62-2P, (2S)-2-[(1S)-5-[2-[2-[4-(3,5-Dimethyl-4-isoxazolyl)phenyl]-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-63-3P, (2S)-2-[(1S)-5-[2-[2-(4-Iodophenyl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-64-4P, (2S)-2-[(1S)-5-[2-[1,4-Dimethyl-2-(4-propylphenyl)-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-65-5P, (2S)-2-[(1S)-5-[2-[2-(1,1'-Biphenyl-3-yl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-66-6P, (2S)-2-[(1S)-5-[2-[1,4-Dimethyl-2-(3'-methyl-1,1'-biphenyl-3-yl)-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-67-7P, (2S)-2-[(1S)-5-[2-[2-[3-(1,3-

Benzodioxol-5-yl)phenyl]-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-68-8P, (2S)-2-[(1S)-5-[2-[2-(2',4'-Difluoro-1,1'-biphenyl-3-yl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-69-9P, (2S)-2-[(1S)-5-[2-[2-(4'-Ethyl-1,1'-biphenyl-3-yl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-70-2P, (2S)-2-[(1S)-5-[2-[2-(3-Bromophenyl)-1,4-dimethyl-1H-imidazol-5-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoic acid 652982-74-6P, (S)-[5-[2-[3-Phenyl-5-(trifluoromethyl)-1H-pyrazol-1-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-75-7P, (S)-[4-Fluoro-5-[2-[3-phenyl-5-(trifluoromethyl)-1H-pyrazol-1-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-76-8P, (S)-[6-Chloro-5-[2-[3-phenyl-5-(trifluoromethyl)-1H-pyrazol-1-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-78-0P, (S)-[6-Bromo-5-[2-[3-phenyl-5-(trifluoromethyl)-1H-pyrazol-1-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-80-4P, (S)-[5-[2-(5-Ethoxy-3-phenyl-1H-pyrazol-1-yl)ethoxy]-2,3-dihydroinden-1-yl]acetic acid 652982-81-5P, (S)-4-[1-[2-[1-(Carboxymethyl)-2,3-dihydro-1H-inden-5-yl]oxy]ethyl]-5-ethoxy-1H-pyrazol-3-yl]benzoic acid 652982-82-6P, (S)-[5-[2-(4-Fluoro-5-methyl-3-phenyl-1H-pyrazol-1-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-83-7P, (S)-[5-[2-(4-Chloro-5-methyl-3-phenyl-1H-pyrazol-1-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-84-8P, (S)-[5-[2-(4-Bromo-5-methyl-3-phenyl-1H-pyrazol-1-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-85-9P, (S)-[5-[2-[5-Methoxy-3-(4-methoxyphenyl)-1H-pyrazol-1-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-86-0P, (S)-[5-[2-[5-Methoxy-3-[4-(trifluoromethyl)phenyl]-1H-pyrazol-1-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-87-1P, (S)-[5-[2-[4-Fluoro-5-methoxy-3-(4-methoxyphenyl)-1H-pyrazol-1-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-88-2P, (S)-[5-[2-[4-Fluoro-5-methoxy-3-[4-(trifluoromethyl)phenyl]-1H-pyrazol-1-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-89-3P, (S)-[5-[2-[4-Bromo-5-methoxy-3-[4-(trifluoromethyl)phenyl]-1H-pyrazol-1-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-90-6P, (S)-[5-[2-(5-Methyl-3-phenyl-1H-pyrazol-1-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-91-7P, 2-[5-[2-(5-Methyl-3-phenylpyrazol-1-yl)ethoxy]indan-1-yl]butyric acid 652982-92-8P, [4-[2-(5-Methyl-3-phenyl-1H-pyrazol-1-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-96-2P, (S)-[5-[2-[4-(4-tert-Butylphenyl)-3,5-dimethyl-1H-pyrazol-1-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-97-3P, (S)-[5-[2-[4-(4-Methoxyphenyl)-3,5-dimethyl-1H-pyrazol-1-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652982-99-5P, (S)-[5-[2-[3,5-Dimethyl-4-[4-(trifluoromethyl)phenyl]-1H-pyrazol-1-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652983-01-2P, (S)-[5-[2-[4-(1,3-Benzodioxol-5-yl)-3,5-dimethyl-1H-pyrazol-1-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652983-02-3P, (S)-[5-[2-(4-Bromo-3,5-dimethyl-1H-pyrazol-1-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652983-03-4P, (S)-[5-[2-[4-(4-Ethylphenyl)-3,5-dimethyl-1H-pyrazol-1-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652983-04-5P, (S)-[5-[2-(3,5-Dimethyl-1H-pyrazol-1-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652983-05-6P, (S)-4-[1-[2-[1-(Carboxymethyl)-2,3-dihydro-1H-inden-5-yl]oxy]ethyl]-3,5-dimethyl-1H-pyrazol-4-yl]benzoic acid 652983-06-7P, (S)-[5-[2-[3,5-Dimethyl-4-(4-methylphenyl)-1H-pyrazol-1-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652983-07-8P, (S)-[5-[2-[4-(2-Methoxyphenyl)-3,5-dimethyl-1H-pyrazol-1-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652983-08-9P, (S)-[5-[2-[3,5-Dimethyl-4-[3-(trifluoromethyl)phenyl]-1H-pyrazol-1-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652983-09-0P, rel-(2S)-2-[(1S)-6-[2-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-1,2,3,4-tetrahydronaphthalen-1-yl]propanoic acid 652983-13-6P, [6-[2-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydrobenzofuran-3-yl]acetic acid 652983-17-0P, 2-[6-[2-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydrobenzofuran-3-yl]propanoic acid 652983-21-6P, 2-[6-[2-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-

dihydrobenzofuran-3-yl]butanoic acid 654650-48-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)

IT 62-56-6, Thiourea, reactions 76-83-5, Triphenylmethyl chloride 94-02-0, Ethyl benzoylacetate 98-80-6, Phenylboronic acid 100-39-0, Benzyl bromide 100-46-9, Benzylamine, reactions 103-71-9, Phenyl isocyanate, reactions 105-36-2, Ethyl bromoacetate 108-59-8, Dimethyl malonate 109-84-2, 2-Hydroxyethylhydrazine 122-01-0, 4-Chlorobenzoyl chloride 326-06-7 420-04-2, Cyanamide 533-68-6, Ethyl  $\alpha$ -bromobutyrate 543-27-1, Isobutyl chloroformate 586-75-4, p-Bromobenzoyl chloride 645-45-4, 3-Phenylpropionyl chloride 667-27-6, Ethyl bromodifluoroacetate 867-13-0, Triethyl phosphonoacetate 1078-19-9, 6-Methoxy-1-tetralone 1487-15-6, 4,5-Dihydro-2-methylfuran 2627-86-3, (S)-(-)- $\alpha$ -Methylbenzylamine 2719-27-9, Cyclohexanecarbonyl chloride 2881-83-6, Ethyl 3-(4-methoxyphenyl)-3-oxopropanoate 3196-15-4, Methyl  $\alpha$ -bromobutyrate 3470-49-3, 5-Hydroxy-1-indanone 3757-88-8, Tributyl(phenylethynyl)tin 3886-69-9, (R)-(+)- $\alpha$ -Methylbenzylamine 5111-70-6, 5-Methoxy-1-indanone 5445-17-0, Methyl 2-bromopropionate 5530-41-6, 6-Methoxy-1,1-dimethylindane 5720-05-8, 4-Methylphenylboronic acid 6272-26-0, 6-Hydroxy-2H-benzofuran-3-one 7486-35-3, Vinyltributyltin 13336-31-7, 4-Methoxy-1-indanone 16909-11-8, 3-(3,5-Dimethoxyphenyl)-2-propenoic acid 17325-26-7 21900-33-4, 3-Bromo-4-methylbenzoyl chloride 24677-78-9, 2,3-Dihydroxybenzaldehyde 25267-28-1, Iodopentane 30414-53-0, Methyl propionylacetate 55499-43-9, 3,4-Dimethylphenylboronic acid 55499-44-0, 2,4-Dimethylphenylboronic acid 58757-38-3, 6-Chloronicotinoyl chloride 63139-21-9, 4-Ethylphenylboronic acid 103788-61-0, 4-(Chloromethyl)-5-methyl-2-phenyl-1,3-oxazole 103788-65-4, 2-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)ethanol 123324-71-0, 4-tert-Butylphenylboronic acid 144432-85-9, 3-Chloro-4-fluorophenylboronic acid 175137-54-9, Ethyl [4-bromo-3,5-dimethyl-1H-pyrazol-1-yl]acetate 251456-48-1, L-Aspartic acid methyl ester hydrochloride 258346-66-6, 2-[2-(4-Fluorophenyl)-5-methyl-1,3-thiazol-4-yl]ethanol 652980-35-3, Methyl (S)-3-[(3-bromo-4-methylbenzoyl)amino]-4-oxopentanoate 652980-44-4, (S)-[5-[2-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetic acid 652980-69-3, Ethyl (S)-[5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652981-81-2, 5-[2-[(tert-Butyldiphenylsilyl)oxy]ethyl]-2-iodo-4-methyl-1-trityl-1H-imidazole

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)

IT 717-94-2P, 3-(3,5-Dimethoxyphenyl)propanoic acid 880-87-5P, 5,7-Dimethoxy-1-indanone 38067-30-0P, 2-(2-Amino-5-methyl-1,3-thiazol-4-yl)ethanol 54732-98-8P, 4-(2-Hydroxyethyl)-5-methyl-1H-imidazole 60812-53-5P, 5-Methoxy-3,3-dimethyl-1-indanone 66495-88-3P, 3-Hydroxy-2-methoxybenzaldehyde 67056-21-7P, 2-(2-Hydroxyethyl)-5-phenyl-2,4-dihydro-3H-pyrazol-3-one 73809-30-0P 76842-70-1P, 7-Hydroxy-5-methoxy-1-indanone 80370-87-2P, (5-Methoxy-2,3-dihydro-1H-inden-1-yl)acetic acid 105983-77-5P, Methyl 4-bromo-3-oxopentanoate 139149-21-6P, 6-(Benzyloxy)benzofuran-3(2H)-one 162713-88-4P, Ethyl (5-methoxy-2,3-dihydro-1H-inden-1-yl)acetate 258346-53-1P, 3-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)-1-propanol 258346-55-3P, 3-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)propanoic acid 259654-73-4P, Methyl (2-amino-5-methyl-1,3-thiazol-4-yl)acetate 478540-95-3P, Methyl [2-(6-chloro-3-pyridinyl)-5-methyl-1,3-oxazol-4-yl]acetate 478540-96-4P, 2-[2-(6-Chloro-3-pyridinyl)-5-methyl-1,3-oxazol-

4-yl]ethanol 496060-58-3P, Methyl 2-(6-methoxy-1H-inden-3-yl)butanoate  
496060-59-4P, 2-(6-Methoxy-1H-inden-3-yl)butanoic acid 496060-60-7P,  
(S)-2-(6-Methoxy-1H-inden-3-yl)butanoic acid 496060-61-8P,  
(2S)-2-((1S)-5-Methoxy-2,3-dihydro-1H-indene-1-yl)butanoic acid  
496060-63-0P, Methyl (2S)-2-((1S)-5-methoxy-2,3-dihydro-1H-indene-1-  
yl)butanoate 496060-64-1P, Methyl (2S)-2-((1S)-5-hydroxy-2,3-dihydro-1H-  
indene-1-yl)butanoate 496061-78-0P, (S)-(5-Methoxy-2,3-dihydro-1H-inden-  
1-yl)acetic acid 496061-79-1P, Ethyl (S)-(5-methoxy-2,3-dihydro-1H-inden-  
1-yl)acetate 496061-80-4P, Ethyl (S)-(5-hydroxy-2,3-dihydro-1H-inden-1-  
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496062-94-3P 496062-95-4P 496063-15-1P, Methyl 2-(5-hydroxy-2,3-  
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2-(5-Ethoxy-3-phenyl-1H-pyrazol-1-yl)ethanol 521084-22-0P, Methyl  
1-pentyl-1H-imidazole 4-carboxylate 521084-23-1P, Methyl  
1-pentyl-1H-imidazole 5-carboxylate 528879-70-1P, 2-(6-Methoxy-3,4-  
dihydronaphthalen-1-yl)propanoic acid 528879-71-2P, rel-(2S)-2-((1S)-6-  
Methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)propanoic acid 528879-72-3P,  
rel-Methyl (2S)-2-((1S)-6-methoxy-1,2,3,4-tetrahydronaphthalen-1-  
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619298-80-5P, (2S)-2-((1S)-5-Methoxy-2,3-dihydro-1H-indene-1-yl)propanoic  
acid 619298-82-7P, Methyl (2S)-2-((1S)-5-methoxy-2,3-dihydro-1H-indene-1-  
yl)propanoate 619298-84-9P 619298-90-7P, Methyl [2-(3-bromo-4-  
methylphenyl)-5-methyl-1,3-oxazol-4-yl]acetate 619298-91-8P,  
2-[2-(3-Bromo-4-methylphenyl)-5-methyl-1,3-oxazol-4-yl]ethanol  
619300-61-7P 652980-32-0P, Methyl (2R)-2-((1R)-5-hydroxy-2,3-dihydro-1H-  
indene-1-yl)propanoate 652980-33-1P, (2R)-2-((1R)-5-Methoxy-2,3-dihydro-  
1H-indene-1-yl)propanoic acid 652980-34-2P, Methyl (2R)-2-((1R)-5-  
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4-(3-Chloropropyl)-5-methyl-2-phenyl-1,3-oxazole 652980-37-5P, Dimethyl  
2-[(5-methyl-2-phenyl-1,3-oxazol-4-yl)methyl]malonate 652980-52-4P,  
Ethyl difluoro(1-hydroxy-5-methoxy-2,3-dihydro-1H-inden-1-yl)acetate  
652980-53-5P, Ethyl difluoro(6-methoxy-1H-inden-3-yl)acetate  
652980-54-6P, Ethyl difluoro(5-methoxy-2,3-dihydro-1H-inden-1-yl)acetate  
652980-55-7P, Ethyl difluoro(5-hydroxy-2,3-dihydro-1H-inden-1-yl)acetate  
652980-59-1P, Ethyl 2-(6-methoxy-1,1-dimethyl-1H-inden-3-yl)butanoate  
652980-60-4P, 2-(6-Methoxy-1,1-dimethyl-1H-inden-3-yl)butanoic acid  
652980-61-5P, rel-(2S)-2-((1S)-5-Methoxy-3,3-dimethyl-2,3-dihydro-1H-  
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methoxy-3,3-dimethyl-2,3-dihydro-1H-indene-1-yl)butanoate 652980-63-7P,  
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yl)butanoate 652980-66-0P, Methyl [3,3-dimethyl-5-[2-(5-methyl-2-phenyl-  
1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652980-68-2P,  
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yl]acetate 652980-81-9P, 5-[2-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-  
1-indanone 652980-82-0P, 2-Methyl-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-  
yl)ethoxy]-1-indanone 652980-83-1P, 2-Methoxy-3-[2-(5-methyl-2-phenyl-  
1,3-oxazol-4-yl)ethoxy]benzaldehyde 652980-84-2P, Ethyl  
3-[2-methoxy-3-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]phenyl]-2-  
propenoate 652980-85-3P, Ethyl 3-[2-methoxy-3-[2-(5-methyl-2-phenyl-1,3-  
oxazol-4-yl)ethoxy]phenyl]propanoate 652980-86-4P, 3-[2-Methoxy-3-[2-(5-  
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652980-87-5P, 4-Methoxy-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-1-  
indanone 652980-88-6P 652980-89-7P, Ethyl [4-methoxy-5-[2-(5-methyl-2-  
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652980-90-0P, Ethyl [4-hydroxy-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-  
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[5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-4-  
-[(trifluoromethyl)sulfonyl]oxy]-2,3-dihydro-1H-inden-1-yl]acetate

652980-92-2P, Ethyl [4-(4-ethylphenyl)-5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652980-99-9P, Ethyl [5-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-7-[[trifluoromethyl)sulfonyl]oxy]-2,3-dihydro-1H-inden-1-yl]acetate 652981-01-6P, 7-(Benzyloxy)-5-methoxy-1-indanone 652981-02-7P, Ethyl [7-(benzyloxy)-5-methoxy-2,3-dihydro-1H-inden-1-ylidene]ethanoate 652981-03-8P, Ethyl (7-hydroxy-5-methoxy-2,3-dihydro-1H-inden-1-yl)acetate 652981-04-9P, Ethyl [5-hydroxy-7-[[trifluoromethyl)sulfonyl]oxy]-2,3-dihydro-1H-inden-1-yl]acetate 652981-29-8P, (S)-[2-(4-Chlorophenyl)-5-oxo-4,5-dihydrooxazol-4-yl]acetic acid methyl ester 652981-30-1P, [2-(4-Chlorophenyl)-5-phenethyloxazol-4-yl]acetic acid methyl ester 652981-31-2P, 2-[2-(4-Chlorophenyl)-5-phenethyloxazol-4-yl]ethanol 652981-40-3P, 2-[5-Methyl-2-(6-phenyl-3-pyridinyl)-1,3-oxazol-4-yl]ethanol 652981-41-4P, Ethyl (S)-[5-[2-[5-methyl-2-(6-phenyl-3-pyridinyl)-1,3-oxazol-4-yl]ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652981-43-6P, Methyl (2S)-2-[(1S)-5-[2-[5-methyl-2-(6-phenyl-3-pyridinyl)-1,3-oxazol-4-yl]ethoxy]-2,3-dihydro-1H-indene-1-yl]propanoate 652981-44-7P, [2-[(tert-Butoxycarbonyl)amino]-5-methyl-1,3-thiazol-4-yl]acetic acid 652981-45-8P, tert-Butyl [4-(2-hydroxyethyl)-5-methyl-1,3-thiazol-2-yl]carbamate 652981-46-9P, Ethyl (S)-[5-[2-(2-amino-5-methyl-1,3-thiazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652981-77-6P 652981-78-7P, 4-[2-[(tert-Butyldiphenylsilyl)oxy]ethyl]-5-methyl-1-trityl-1H-imidazole 652981-79-8P, 4-[2-[(tert-Butyldiphenylsilyl)oxy]ethyl]-2-iodo-5-methyl-1-trityl-1H-imidazole 652981-80-1P, 2-(2-Iodo-5-methyl-1-trityl-1H-imidazol-4-yl)ethanol 652981-83-4P, Ethyl (S)-[5-[2-(2-iodo-5-methyl-1-trityl-1H-imidazol-4-yl)ethoxy]-2,3-dihydro-1H-inden-1-yl]acetate 652981-88-9P, 2-(1,4-Dimethyl-2-phenyl-1H-imidazol-5-yl)ethanol 652981-89-0P, 5-[2-[(tert-Butyldiphenylsilyl)oxy]ethyl]-2-iodo-4-methyl-1H-imidazole 652981-90-3P, 5-[2-[(tert-Butyldiphenylsilyl)oxy]ethyl]-2-iodo-1,4-dimethyl-1H-imidazole 652981-91-4P, 4-[2-[(tert-Butyldiphenylsilyl)oxy]ethyl]-2-iodo-1,5-dimethyl-1H-imidazole 652981-92-5P, 4-[2-[(tert-Butyldiphenylsilyl)oxy]ethyl]-1,5-dimethyl-2-phenyl-1H-imidazole 652981-93-6P, 5-[2-[(tert-Butyldiphenylsilyl)oxy]ethyl]-1,4-dimethyl-2-phenyl-1H-imidazole 652982-14-4P, (2-Bromo-1-pentyl-1H-imidazol-5-yl)methanol 652982-15-5P, Methyl 2-bromo-1-pentyl-1H-imidazole-5-carboxylate 652982-24-6P, Methyl (S)-3-[(4-bromobenzoyl)amino]-4-oxopentanoate 652982-25-7P, Methyl (S)-3-[(4-bromobenzoyl)(methyl)amino]-4-oxopentanoate 652982-26-8P, Methyl [2-(4-bromophenyl)-1,4-dimethyl-1H-imidazol-5-yl]acetate 652982-27-9P, 2-[2-(4-Bromophenyl)-1,4-dimethyl-1H-imidazol-5-yl]ethanol 652982-71-3P, 2-[5-Methoxy-3-(4-methoxyphenyl)-1H-pyrazol-1-yl]ethanol 652982-72-4P, 2-(5-Trifluoromethyl-3-phenyl-1H-pyrazol-1-yl)ethanol 652982-77-9P, Ethyl (S)-2-[6-chloro-5-[2-[3-phenyl-5-(trifluoromethyl)pyrazol-1-yl]ethoxy]indan-1-yl]acetate 652982-79-1P, Ethyl (S)-2-[6-bromo-5-[2-[3-phenyl-5-(trifluoromethyl)pyrazolyl]ethoxy]indan-1-yl]acetate 652982-93-9P, 2-(4-Bromo-3,5-dimethyl-1H-pyrazol-1-yl)ethanol 652983-10-3P, Methyl 2-(6-methoxy-3,4-dihydronaphthalen-1-yl)propanoate 652983-11-4P, rel-Methyl (2S)-2-[(1S)-6-hydroxy-1,2,3,4-tetrahydronaphthalen-1-yl]propanoate 652983-12-5P, rel-Methyl (2S)-2-[(1S)-6-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-1,2,3,4-tetrahydronaphthalen-1-yl]propanoate 652983-14-7P, Ethyl [6-(benzyloxy)benzofuran-3-yl]acetate 652983-15-8P, Ethyl (6-hydroxy-2,3-dihydrobenzofuran-3-yl)acetate 652983-16-9P, Ethyl [6-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydrobenzofuran-3-yl]acetate 652983-18-1P, Methyl 2-[6-(benzyloxy)benzofuran-3-yl]propanoate 652983-19-2P, Methyl 2-(6-hydroxy-2,3-dihydrobenzofuran-3-yl)propanoate 652983-20-5P, Methyl 2-[6-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydrobenzofuran-3-yl]propanoate 652983-22-7P, Methyl 2-[6-(benzyloxy)benzofuran-3-yl]butanoate 652983-23-8P, Methyl 2-(6-hydroxy-2,3-dihydrobenzofuran-3-yl)butanoate 652983-24-9P, Methyl

2-[6-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-2,3-dihydrobenzofuran-3-yl]butanoate

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)

IT 50-99-7, Glucose, biological studies

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(tolerance; preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Alisa, B; WO 0218355 A 2002 HCAPLUS

(2) Bayer Pharmaceuticals Corporation; WO 03089418 A 2003 HCAPLUS

(3) Ono Pharmaceutical Co; WO 02051820 A 2002 HCAPLUS

(4) Ono Pharmaceutical Co; EP 1354879 A 2003 HCAPLUS

(5) Pfizer; WO 9119702 A 1991 HCAPLUS

(6) Stolle, A; WO 03011842 A 2003 HCAPLUS

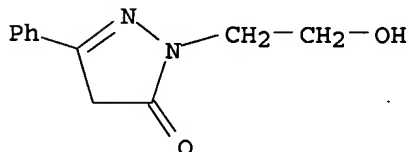
IT 67056-21-7P, 2-(2-Hydroxyethyl)-5-phenyl-2,4-dihydro-3H-pyrazol-3-one

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of indane, dihydrobenzofuran and tetrahydronaphthalene carboxylic acid derivs. as antidiabetic agents)

RN 67056-21-7 HCAPLUS

CN 3H-Pyrazol-3-one, 2,4-dihydro-2-(2-hydroxyethyl)-5-phenyl- (9CI) (CA INDEX NAME)



L85 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:922570 HCAPLUS

DN 139:391386

ED Entered STN: 26 Nov 2003

TI Pyrazolone analogs for repairing fibrosis tissues

IN Chiba, Akira; Matsumoto, Hideki; Tanaka, Yasuhiro; Ijichi, Chiori; Oomuta, Naoko; Takatsuki, Fumihiko

PA Ajinomoto Co., Inc., Japan

SO Jpn. Kokai Tokkyo Koho, 14 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

IC ICM A61K031-4152

ICS A61K007-00; A61K007-48; A61P001-16; A61P009-08; A61P009-10;  
A61P011-00; A61P013-08; A61P013-12; A61P017-02; A61P037-00;  
A61P043-00; C07D231-20; C07D231-22; C07D231-26; C07D231-38

CC 1-12 (Pharmacology)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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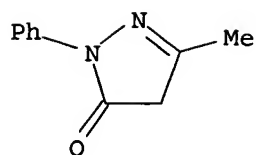
PRAI JP 2002-144719

20020520 &lt;--

## CLASS

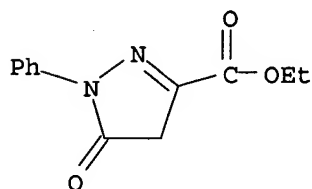
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AB		Pyrazolone analogs (Markush's structure given) and their pharmaceutically acceptable salts are claimed for repairing fibrosis tissues, including liver, lung, and kidney fibrosis, atherosclerosis, systemic sclerosis, liver cirrhosis, prostatomegaly symptom, keloid, scar, myocardial disease, ischemia, and collagen disease.
ST		pyrazolone analog tissue fibrosis
IT		Prostate gland, disease (benign hyperplasia; pyrazolone analogs for repairing fibrosis tissues)
IT		Hyperplasia (benign prostatic; pyrazolone analogs for repairing fibrosis tissues)
IT		Kidney, disease Liver, disease Lung, disease (fibrosis; pyrazolone analogs for repairing fibrosis tissues)
IT		Fibrosis (hepatic; pyrazolone analogs for repairing fibrosis tissues)
IT		Fibrosis (pulmonary; pyrazolone analogs for repairing fibrosis tissues)
IT		Anti-ischemic agents Atherosclerosis Cirrhosis Connective tissue, disease Fibrosis Heart, disease Keloid (pyrazolone analogs for repairing fibrosis tissues)
IT		Collagen fibers RL: BSU (Biological study, unclassified); BIOL (Biological study) (pyrazolone analogs for repairing fibrosis tissues)
IT		Fibrosis (renal; pyrazolone analogs for repairing fibrosis tissues)
IT		Skin, disease (scar; pyrazolone analogs for repairing fibrosis tissues)
IT		Connective tissue, disease (scleroderma; pyrazolone analogs for repairing fibrosis tissues)
IT		89-25-8 89-33-8 321-07-3 1691-93-6 2749-59-9 4149-06-8 4551-69-3 39455-90-8D, Pyrazolone, analogs and salts 51686-30-7 66076-81-1 87031-30-9 132214-71-2 300588-64-1 468743-27-3 625382-74-3 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pyrazolone analogs for repairing fibrosis tissues)
IT		89-25-8 89-33-8 2749-59-9 87031-30-9 132214-71-2 300588-64-1 625382-74-3 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pyrazolone analogs for repairing fibrosis tissues)
RN		89-25-8 HCAPLUS
CN		3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (9CI) (CA INDEX NAME)





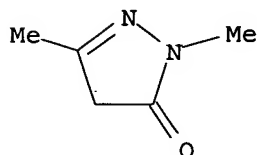
RN 89-33-8 HCAPLUS

CN 1H-Pyrazole-3-carboxylic acid, 4,5-dihydro-5-oxo-1-phenyl-, ethyl ester  
(9CI) (CA INDEX NAME)



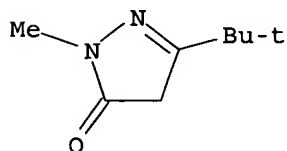
RN 2749-59-9 HCAPLUS

CN 3H-Pyrazol-3-one, 2,4-dihydro-2,5-dimethyl- (9CI) (CA INDEX NAME)



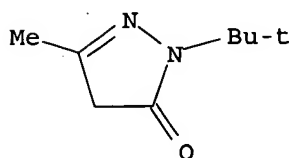
RN 87031-30-9 HCAPLUS

CN 3H-Pyrazol-3-one, 5-(1,1-dimethylethyl)-2,4-dihydro-2-methyl- (9CI) (CA INDEX NAME)

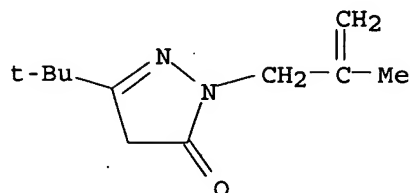


RN 132214-71-2 HCAPLUS

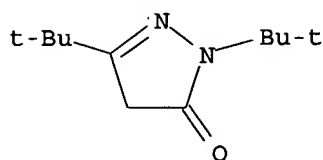
CN 3H-Pyrazol-3-one, 2-(1,1-dimethylethyl)-2,4-dihydro-5-methyl- (9CI) (CA INDEX NAME)



RN 300588-64-1 HCAPLUS  
 CN 3H-Pyrazol-3-one, 5-(1,1-dimethylethyl)-2,4-dihydro-2-(2-methyl-2-propenyl)- (9CI) (CA INDEX NAME)



RN 625382-74-3 HCAPLUS  
 CN 3H-Pyrazol-3-one, 2,5-bis(1,1-dimethylethyl)-2,4-dihydro- (9CI) (CA INDEX NAME)



L85 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2003:921440 HCAPLUS  
 DN 139:391385  
 ED Entered STN: 25 Nov 2003  
 TI Pyrazolone analogs for repairing tissue fibrosis  
 IN Chiba, Akira; Matsumoto, Hideki; Tanaka, Yasuhiro; Ijichi, Chiori; Oomuta, Naoko; Takatsuki, Fumihiko  
 PA Ajinomoto Co., Inc., Japan  
 SO Jpn. Kokai Tokkyo Koho, 10 pp.  
 CODEN: JKXXAF  
 DT Patent  
 LA Japanese  
 IC ICM A61K031-4152  
 ICS A61K031-4155; A61K031-4196; A61K031-4439; A61P001-16; A61P009-00; A61P009-10; A61P011-00; A61P013-08; A61P013-12; A61P017-02; A61P019-02; A61P037-00; A61P041-00; A61P043-00; C07D231-26; C07D231-28; C07D231-52; C07D401-04; C07D403-04  
 CC 1-12 (Pharmacology)

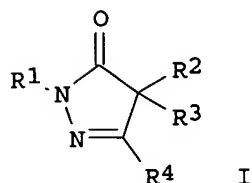
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PRAI JP 2002-144720		20020520	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
JP 2003335672	ICM	A61K031-4152
	ICS	A61K031-4155; A61K031-4196; A61K031-4439; A61P001-16; A61P009-00; A61P009-10; A61P011-00; A61P013-08; A61P013-12; A61P017-02; A61P019-02; A61P037-00; A61P041-00; A61P043-00; C07D231-26; C07D231-28; C07D231-52; C07D401-04; C07D403-04

OS MARPAT 139:391385  
GI



AB Pyrazolone analogs (I; R1 = (substituted)phenyl; R2, R3 = H; R4 = low alkyl, alkoxy, etc.) and their pharmaceutically acceptable salts are claimed for repairing tissue fibrosis, including liver fibrosis, lung fibrosis, kidney fibrosis, atherosclerosis, prostate hypertrophy, keloid symptom, myocardial symptom, and collagen disease.

ST pyrazolone analog tissue fibrosis

IT Prostate gland, disease  
(benign hyperplasia; pyrazolone analogs for repairing tissue fibrosis)

IT Hyperplasia  
(benign prostatic; pyrazolone analogs for repairing tissue fibrosis)

IT Kidney, disease  
Liver, disease  
Lung, disease  
(fibrosis; pyrazolone analogs for repairing tissue fibrosis)

IT Fibrosis  
(hepatic; pyrazolone analogs for repairing tissue fibrosis)

IT Fibrosis  
(pulmonary; pyrazolone analogs for repairing tissue fibrosis)

IT **Atherosclerosis**  
Connective tissue, disease  
Fibrosis  
Heart, disease  
Ischemia  
Keloid  
Respiratory tract, disease  
(pyrazolone analogs for repairing tissue fibrosis)

IT Collagen fibers  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(pyrazolone analogs for repairing tissue fibrosis)

IT Fibrosis  
(renal; pyrazolone analogs for repairing tissue fibrosis)

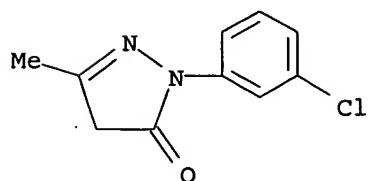
IT 90-31-3 4845-49-2 6402-09-1 6631-89-6  
13024-90-3 17900-68-4 24515-10-4 27241-32-3  
29211-43-6 30818-17-8 132214-72-3 406193-37-1  
626201-75-0  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(pyrazolone analogs for repairing tissue fibrosis)

IT 90-31-3 4845-49-2 6402-09-1 6631-89-6  
13024-90-3 17900-68-4 29211-43-6  
30818-17-8  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(pyrazolone analogs for repairing tissue fibrosis)

RN 90-31-3 HCAPLUS

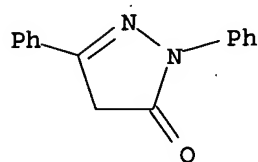
CN 3H-Pyrazol-3-one, 2-(3-chlorophenyl)-2,4-dihydro-5-methyl- (9CI) (CA

INDEX NAME)



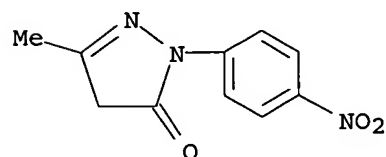
RN 4845-49-2 HCAPLUS

CN 3H-Pyrazol-3-one, 2,4-dihydro-2,5-diphenyl- (9CI) (CA INDEX NAME)



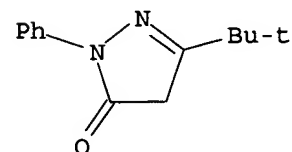
RN 6402-09-1 HCAPLUS

CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



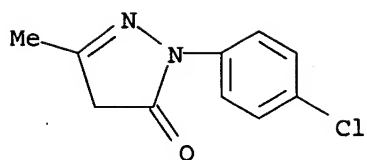
RN 6631-89-6 HCAPLUS

CN 3H-Pyrazol-3-one, 5-(1,1-dimethylethyl)-2,4-dihydro-2-phenyl- (9CI) (CA INDEX NAME)

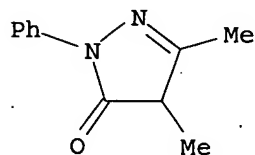


RN 13024-90-3 HCAPLUS

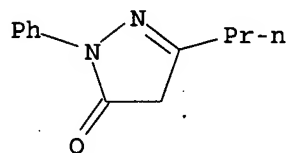
CN 3H-Pyrazol-3-one, 2-(4-chlorophenyl)-2,4-dihydro-5-methyl- (9CI) (CA INDEX NAME)



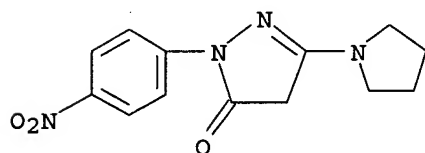
RN 17900-68-4 HCAPLUS  
CN 3H-Pyrazol-3-one, 2,4-dihydro-4,5-dimethyl-2-phenyl- (9CI) (CA INDEX NAME)



RN 29211-43-6 HCAPLUS  
CN 3H-Pyrazol-3-one, 2,4-dihydro-2-phenyl-5-propyl- (9CI) (CA INDEX NAME)



RN 30818-17-8 HCAPLUS  
CN 3H-Pyrazol-3-one, 2,4-dihydro-2-(4-nitrophenyl)-5-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



L85 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:355610 HCAPLUS  
DN 138:348714  
ED Entered STN: 09 May 2003  
TI Use of peroxyxynitrite scavengers or peroxyxynitrite formation inhibitors that do not diminish nitric oxide synthesis or activity to reverse or prevent premature vascular senescence  
IN Goligorsky, Michael S.; Chen, Jun  
PA USA  
SO U.S. Pat. Appl. Publ., 11 pp.  
CODEN: USXXCO  
DT Patent

LA English  
 IC ICM A61K038-44  
 ICS A61K031-555; A61K031-445; A61K031-416; A61K031-353; A61K031-198;  
 A61K031-192; A61K035-78

INCL 424094400; 514185000; 514410000; 514327000; 514407000; 514456000;  
 514561000; 424769000; 514569000; 514562000

CC 1-8 (Pharmacology)  
 Section cross-reference(s): 9

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003086916	A1	20030508	US 2002-269032	20021011 <--
	US 2005113427	A1	20050526	US 2004-13457	20041217 <--
PRAI	US 2001-329010P	P	20011012	<--	
	US 2002-269032	A1	20021011		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2003086916	ICM	A61K038-44
	ICS	A61K031-555; A61K031-445; A61K031-416; A61K031-353; A61K031-198; A61K031-192; A61K035-78
	INCL	424094400; 514185000; 514410000; 514327000; 514407000; 514456000; 514561000; 424769000; 514569000; 514562000
US 2003086916	NCL	424/094.400; 514/185.000; 514/410.000; 514/327.000; 514/407.000; 514/456.000; 514/561.000; 424/769.000; 514/569.000; 514/562.000
	ECLA	A61K031/00; A61K031/192; A61K031/192+M; A61K031/198; A61K031/198+M; A61K031/353; A61K031/353+M; A61K031/416; A61K031/416+M; A61K031/445; A61K031/445+M; A61K031/555; A61K031/555+M; A61K045/06 <--
US 2005113427	NCL	514/359.000
	ECLA	A61K031/00; A61K031/192; A61K031/192+M; A61K031/198; A61K031/198+M; A61K031/353; A61K031/353+M; A61K031/416; A61K031/416+M; A61K031/445; A61K031/445+M; A61K031/555; A61K031/555+M; A61K045/06 <--

AB Premature vascular senescence is reversed or prevented in tissue or cells by contacting the tissue or cells with a peroxynitrite scavenger or peroxynitrite formation inhibitor that does not diminish nitric oxide synthesis. This finds application in treatment of patients with a disorder associated with elevated levels of advanced glycation end products in blood or tissue, e.g., patients with end stage renal disease or poorly controlled diabetes, and in contacting vascular tissue or cells ex vivo to prevent occurrence of premature senescence. Human umbilical vein endothelial cells (HUVEC) after four passages were plated on glycated collagen with or without the addition of 0.1 mM ebselen. Ebselen was able to reverse premature senescence at all dilns. of glycated collagen.

ST peroxynitrite scavenger reverse premature vascular senescence; ebselen reversal premature senescence HUVEC cell; glycated collagen premature senescence HUVEC cell ebselen

IT Glycoproteins

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
 (AGE (advanced glycosylation end product), treatment of patients with; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)

IT Animal cell line

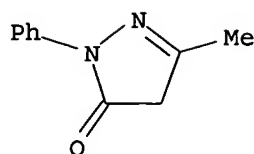
(HUVEC, ebselen reversal of premature senescence of; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature

- vascular senescence)
- IT Transplant and Transplantation  
(allotransplant, treatment of cells or tissue seeded onto; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Artery  
Blood vessel  
(artificial, treatment of cells or tissue seeded onto; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Kidney, disease  
(chronic, treatment of; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Nervous system, disease  
(degeneration, treatment of; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Kidney, disease  
(failure, chronic, irreversible, treatment of; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Drug delivery systems  
(liposomes, cationic, with entrapped superoxide dismutase; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Radical scavengers  
(of peroxynitrite; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Blood vessel, disease  
(peripheral, treatment of; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Animal  
Animal tissue culture  
Anti-Alzheimer's agents  
Antidiabetic agents  
Human  
(peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Flavonoids  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Carboxylic acids, biological studies  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(phenolic; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Embryophyta  
(polyphenols of; peroxynitrite scavengers or peroxynitrite formation

- inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Phenols, biological studies  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(polyphenols, nonpolymeric; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Blood vessel, disease  
(premature senescence; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Cell aging  
(premature vascular; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Polyoxalkylenes, biological studies  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(reaction products with superoxide dismutase; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Medical goods  
(stents, treatment of cells or tissue seeded onto; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Lupus erythematosus  
(systemic, treatment of; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Animal tissue  
Blood  
(treatment of patients with advanced glycation end products in; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Diabetes mellitus  
(treatment of poorly controlled; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Alzheimer's disease  
(treatment of; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Heart  
(valve, artificial, treatment of cells or tissue seeded onto; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT Transplant and Transplantation  
(xenotransplant, treatment of cells or tissue seeded onto; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT 469-32-9, Hamamelitannin  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)



- (bark exts. containing; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT 9054-89-1D, C-terminal glycine and arginine tail-containing  
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (copper-zinc-containing; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT 19059-14-4, Peroxynitrite  
 RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
 (peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT 10102-43-9, Nitric oxide, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT 52-90-4D, L-Cysteine, substituted with tellurium or selenium 56-89-3D, L-Cystine, substituted with tellurium or selenium 63-68-3D, Methionine, substituted with tellurium or selenium 69-93-2, Uric acid, biological studies 89-25-8, 3-Methyl-1-phenyl-2-pyrazolin-5-one  
 94-93-9D, Salen, manganese complexes 101-60-0D, Porphyrin, manganese complexes 117-39-5, Quercetin 124-09-4D, Hexamethylenediamine, conjugates with superoxide dismutase 327-97-9, Chlorogenic acid 331-39-5, Caffeic acid 530-59-6, Sinapic acid 635-78-9, Resorufin 1135-24-6, Ferulic acid 2226-96-2 7782-49-2D, Selenium, cystine or cysteine or methionine compds. 9054-89-1D, Superoxide dismutase, conjugates with hexamethylenediamine or reaction products with PEG 13494-80-9D, Tellurium, cystine or cysteine or methionine compds. 16397-91-4D, Manganese II, complexes with bis(cyclohexylpyridine)-substituted macrocyclic ligand, biological studies 25322-68-3D, Polyethylene glycol, reaction products with superoxide dismutase 53054-07-2, N $\omega$ -Hydroxy-L-arginine 55266-18-7 60489-13-6, 5,10,15,20-Tetrakis(N-methyl-4'-pyridyl)porphyrinato iron (III) 60940-34-3, Ebselen 139028-97-0, 5,10,15,20-Tetrakis(2,4,6-trimethyl-3,5-disulfonatophenyl)porphyrinato iron (III) 223723-79-3 256474-80-3  
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- IT 89-25-8, 3-Methyl-1-phenyl-2-pyrazolin-5-one  
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing nitric oxide synthesis or activity for reversing or preventing premature vascular senescence)
- RN 89-25-8 HCAPLUS  
 CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl-, (9CI) (CA INDEX NAME)



L85 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2002:240746 HCAPLUS  
 DN 136:279468  
 ED Entered STN: 28 Mar 2002  
 TI Preparation of 4-amino-quinazolines useful as glycoprotein IbIX  
 antagonists, and their use for control of thrombotic disorders  
 IN Mederski, Werner; Devant, Ralf; Barnickel, Gerhard; Bernotat-Danielowski,  
 Sabine; Vickers, James; Cezanne, Bertram; Dhanoa, Daljit; Zhao, Bao-Ping;  
 Rinker, James; Player, Mark R.; Jaeger, Edward; Soll, Richard  
 PA Merck Patent G.m.b.H., Germany  
 SO PCT Int. Appl., 83 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07D239-94  
 ICS C07D239-95; C07D403-12; C07D405-12; C07D409-14; C07D401-12;  
 C07D409-04; A61K031-517; A61P009-10  
 CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))  
 Section cross-reference(s): 1, 63

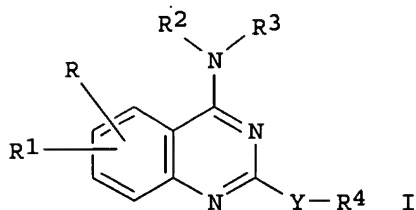
FAN.CNT 1

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WO 2002024667	A1	20020328	WO 2001-EP10705	20010917 <--
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CA 2422488	AA	20020328	CA 2001-2422488	20010917 <--
AU 2001093817	A5	20020402	AU 2001-93817	20010917 <--
EP 1318984	A1	20030618	EP 2001-974258	20010917 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001014020	A	20030722	BR 2001-14020	20010917 <--
JP 2004509876	T2	20040402	JP 2002-529077	20010917 <--
ZA 2003003062	A	20040719	ZA 2003-3062	20030417 <--
PRAI US 2000-666908	A	20000920	<--	
WO 2001-EP10705	W	20010917	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002024667	ICM	C07D239-94
	ICS	C07D239-95; C07D403-12; C07D405-12; C07D409-14; C07D401-12; C07D409-04; A61K031-517; A61P009-10
WO 2002024667	ECLA	C07D239/94; C07D401/12+239+211; C07D403/12+239+209C; C07D405/12+317+239; C07D409/04+333B+239;

C07D409/14+333B+239+209C; C07D409/14+333B+239+211;  
C07D239/95 <--  
JP 2004509876 FTERM 4C063/AA01; 4C063/BB09; 4C063/CC31; 4C063/CC73;  
4C063/CC81; 4C063/CC92; 4C063/DD04; 4C063/DD06;  
4C063/DD12; 4C063/DD15; 4C063/DD22; 4C063/DD25;  
4C063/DD31; 4C063/EE01; 4C086/AA01; 4C086/AA02;  
4C086/AA03; 4C086/AA04; 4C086/BC46; 4C086/GA02;  
4C086/GA04; 4C086/GA07; 4C086/GA08; 4C086/GA12;  
4C086/MA01; 4C086/NA14; 4C086/ZA36; 4C086/ZA40;  
4C086/ZA45; 4C086/ZA54; 4C086/ZC41 <--  
OS MARPAT 136:279468  
GI



AB The preparation of 4-amino-quinazolines [I; wherein R, R1, independently = H, (C1-C6)alkyl, OH, (C1-C6)alkoxy, amino, nitro, cyano, etc.; R2, R3, independently = H, (C1-C6)alkyl, cycloalkyl, mono- or bicycloheterocyclic radical, etc.; R4 = aryl (e.g., Ph, naphthyl, biphenyl, etc.), or thiophen-2-yl substituted with aryl (as described supra) or heterocyclic radical, etc.; each of R, R1-R4 with many provisos] is described. Thus, [2-(4-bromophenyl)-7-chloroquinazolin-4-yl]-phenylamine was prepared by a multistep synthesis. The prepared compds. are useful as glycoprotein IbIX antagonists (no data) for the control of thrombotic disorders and sequelae deriving thereof.

ST aminoquinazoline prepn glycoprotein IbIX antagonist antithrombotic  
IT CD antigens  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(CD42a, complex with Ib; preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT Glycoproteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(GP IX, complex with Ib; preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT Glycoproteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(GPIb, complex with IX; preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT Drug delivery systems  
(capsules; preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT Medical goods  
(catheters, anti-adhesive substances for; preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT **Artery, disease**  
(coronary, occlusion, treatment; preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT **Artery, disease**  
(coronary, restenosis, treatment; preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT Drug delivery systems  
(eye drops; preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT Prosthetic materials and Prosthetics  
(implants, anti-adhesive substances for; preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT Prosthetic materials and Prosthetics  
(implants, artificial heart pacemaker, anti-adhesive substances for; preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT Heart, disease  
(infarction, treatment; preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT Cell adhesion molecules  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT Drug delivery systems  
(injection; preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT Circulation  
(peripheral, disorder, treatment; preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT Anti-ischemic agents  
Antianginal agents  
Antiartherosclerotics  
Anticoagulants  
Human  
(preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT Brain, disease  
(stroke, treatment; preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT Drug delivery systems  
(suppositories; preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT Drug delivery systems  
(tablets, coated and uncoated; preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT Drug delivery systems  
(topical ointment; preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT 405932-32-3P 405932-33-4P 405932-34-5P 405932-35-6P 405932-36-7P  
405932-37-8P 405932-39-0P 405932-41-4P 405932-43-6P 405932-45-8P  
405932-46-9P 405932-47-0P 405932-48-1P 405932-49-2P 405932-50-5P  
405932-51-6P 405932-53-8P 405932-54-9P 405932-55-0P 405932-57-2P  
405932-59-4P 405932-61-8P 405932-63-0P 405932-64-1P 405932-66-3P  
405932-68-5P 405932-70-9P 405932-71-0P 405932-72-1P 405932-73-2P  
405932-74-3P 405932-75-4P 405932-77-6P 405932-78-7P 405932-79-8P  
405932-80-1P 405932-81-2P 405932-82-3P 405932-83-4P 405932-84-5P  
405932-85-6P 405932-86-7P 405932-87-8P 405932-88-9P 405932-89-0P  
405932-90-3P 405932-91-4P 405932-92-5P 405932-93-6P 405932-94-7P  
405932-96-9P 405932-97-0P 405932-98-1P 405932-99-2P 405933-00-8P  
405933-01-9P 405933-02-0P 405933-04-2P 405933-06-4P 405933-08-6P  
405933-10-0P 405933-12-2P 405933-14-4P 405933-16-6P 405933-18-8P  
405933-20-2P 405933-22-4P 405933-23-5P 405933-25-7P 405933-26-8P  
405933-28-0P 405933-29-1P 405933-31-5P 405933-33-7P 405933-35-9P  
405933-37-1P 405933-39-3P 405933-41-7P 405933-43-9P 405933-44-0P  
405933-45-1P 405933-46-2P 405933-48-4P 405933-49-5P 405933-51-9P  
405933-52-0P 405933-53-1P 405933-55-3P 405933-56-4P 405933-57-5P  
405933-58-6P 405933-59-7P 405933-60-0P 405933-61-1P 405933-62-2P  
405933-63-3P 405933-64-4P 405933-65-5P 405933-66-6P 405933-67-7P

405933-68-8P 405933-69-9P 405933-70-2P 405933-71-3P 405933-72-4P  
 405933-73-5P 405933-74-6P 405933-75-7P 405933-76-8P 405933-77-9P  
 405933-78-0P 405933-79-1P 405933-80-4P 405933-81-5P 405933-82-6P  
 405933-83-7P 405933-84-8P 405933-85-9P 405933-86-0P 405933-87-1P  
 405933-88-2P 405933-89-3P 405933-90-6P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT 62-53-3, Aniline, reactions 89-97-4 89-99-6 92-54-6,  
 1-Phenylpiperazine 95-00-1 99-88-7 100-36-7 100-46-9, Benzylamine,  
 reactions 100-60-7 100-82-3 102-49-8 103-67-3 104-13-2  
 104-84-7 104-86-9 108-00-9 109-55-7 109-73-9, Butylamine,  
 reactions 109-85-3 110-58-7, Pentylamine 110-68-9 123-00-2,  
 4-Morpholinepropanamine 139-59-3 140-75-0 140-80-7 578-54-1  
 586-75-4, 4-Bromobenzoyl chloride 587-02-0 589-16-2 618-36-0  
 1125-60-6, 5-Isoquinolinamine 1484-85-1, 1,3-Benzodioxole-5-ethanamine  
 2038-03-1, 4-Morpholineethanamine 2039-67-0 2393-23-9 2524-67-6  
 2579-20-6, 1,3-Cyclohexanedimethanamine 2620-50-0, 1,3-Benzodioxole-5-  
 methanamine 2696-84-6 2706-56-1, 2-Pyridineethanamine 3470-99-3,  
 1-Propylpyrrolidin-2-one 3586-12-7 4543-96-8 4572-03-6 4795-29-3  
 5036-48-6, 1H-Imidazole-1-propanamine 5332-73-0 5763-61-1  
 6402-08-0 6850-57-3 7663-77-6 10372-41-5 13258-63-4,  
 4-Pyridineethanamine 15532-75-9 18638-99-8 22184-97-0 25560-00-3  
 26116-12-1 26455-36-7 27578-60-5, 1-Piperidineethanamine 29026-75-3  
 30433-91-1, 2-Thiopheneethanamine 31252-42-3 38487-86-4,  
 2-Amino-4-chlorobenzonitrile 51135-96-7 51387-90-7 57264-46-7  
 57957-09-2 60035-03-2 61510-27-8 72955-85-2 74788-44-6  
 79467-22-4 177976-50-0 299921-01-0 387350-84-7 387350-86-9  
 405928-19-0 405933-95-1 405933-96-2 405933-97-3,  
 2-(4-Bromophenyl)-4-chloro-6-methylquinazoline 405933-98-4,  
 2-(4-Bromophenyl)-4,6-dichloroquinazoline 405933-99-5,  
 2-(4-Bromophenyl)-4-chloro-6,7-dimethoxyquinazoline 405934-00-1,  
 4-Chloro-2-(4-bromobutyl)quinazoline

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

IT 405933-91-7P, 4-Bromo-N-(5-chloro-2-cyanophenyl)benzamide 405933-92-8P,  
 4-Bromo-N-(5-chloro-2-aminocarbonylphenyl)benzamide 405933-93-9P,  
 2-(4-Bromophenyl)-7-chloro-3H-quinazolin-4-one 405933-94-0P,  
 2-(4-Bromophenyl)-4,7-dichloroquinazoline

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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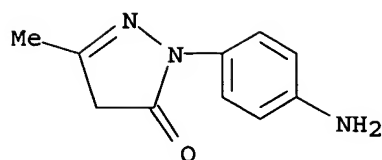
IT 6402-08-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of amino-quinazolines useful as glycoprotein IbIX antagonists)

RN 6402-08-0 HCAPLUS

CN 3H-Pyrazol-3-one, 2-(4-aminophenyl)-2,4-dihydro-5-methyl- (9CI) (CA INDEX  
 NAME)



L85 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:766854 HCAPLUS

DN 130:163082

ED Entered STN: 08 Dec 1998

TI Neuroprotective effects depend on the model of focal ischemia following middle cerebral artery occlusion

AU Takamatsu, Hiroyuki; Kondo, Kazunao; Ikeda, Yasuhiko; Umemura, Kazuo

CS Department of Pharmacology, Hamamatsu University School of Medicine, Hamamatsu, 431-3192, Japan

SO European Journal of Pharmacology (1998), 362(2/3), 137-142

CODEN: EJPHAZ; ISSN: 0014-2999

PB Elsevier Science B.V.

DT Journal

LA English

CC 1-11 (Pharmacology)

AB The purpose of the present study was to compare the characteristics of the photochem.-induced thrombotic occlusion model and the thermocoagulated occlusion model of the middle cerebral artery in rats. We evaluated the neuroprotective effects of a NMDA receptor antagonist, (+)-MK-801 (dizocilpine, (+)-5-methyl-10,11-dihydro-5H-dibenzo[a,d]cycloheptan-5,10-imine), an  $\alpha$ -amino-3-hydroxy-5-methylisoxazole-4-propionic acid receptor antagonist, YM90K (6-(1H-imidazol-1-yl)-7-nitro-2,3(1H,4H)-quinoxalinedione monohydrochloride), a  $\text{Ca}^{2+}$  channel antagonist, S-312-d (S-(+)-methyl-4,7-dihydro-3-isobutyl-6-methyl-4-(3-nitrophenyl)-thieno[2,3-b]pyridine-5-carboxylate), the radical scavengers, MCI-186 (3-methyl-1-phenyl-2-pyrazolin-5-one) and EPC-K1

(1-ascorbic acid 2-[3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2H-1-benzopyran-6yl-hydrogen phosphate] potassium salt), and a calcineurin inhibitor, FK506 (tacrolimus, Prograf). Although all tested agents in the present study attenuated the brain damage in the photochem.-induced thrombotic occlusion model, the radical scavengers did not attenuate the brain damage in the thermocoagulated occlusion model. The time course of brain damage and brain edema formation in the two models was examined. The time course of brain damage was not different in the two models, but the time course of brain edema was quite different. Brain edema formation in the photochem.-induced thrombotic occlusion model was significantly greater ( $P < 0.01$ ) than that in the thermocoagulated occlusion model at all time point studied until 24 h after occlusion of the middle cerebral artery. The present study suggests that the photochem.-induced thrombotic occlusion model has characteristics of both permanent ischemia and ischemia-reperfusion.

ST neuroprotection model focal cerebral ischemia

IT Brain, disease

(ischemia, focal; neuroprotective effects depend on model of focal ischemia following middle cerebral artery occlusion)

IT Artery, disease

Artery, disease

(middle cerebral, occlusion; neuroprotective effects depend on model of focal ischemia following middle cerebral artery

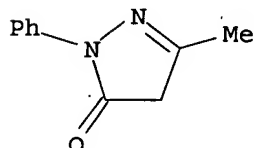
## occlusion)

- IT Cytoprotective agents  
(neuroprotectants; neuroprotective effects depend on model of focal ischemia following middle cerebral artery occlusion)
- IT Anti-ischemic agents  
Disease models  
Drug screening  
(neuroprotective effects depend on model of focal ischemia following middle cerebral artery occlusion)
- IT 89-25-8, MCI-186 77086-21-6, Dizocilpine  
104987-11-3, FK506 120056-57-7 127061-56-7, EPC-K1 154164-30-4,  
YM90K  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(neuroprotective effects depend on model of focal ischemia following middle cerebral artery occlusion)

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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 IT 89-25-8, MCI-186  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (neuroprotective effects depend on model of focal ischemia following middle cerebral artery occlusion)  
 RN 89-25-8 HCAPLUS  
 CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (9CI) (CA INDEX NAME)



L85 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1993:225298 HCAPLUS  
 DN 118:225298  
 ED Entered STN: 12 Jun 1993  
 TI The effects of MCI-186 on ischemic-reperfusion injury during cardiopulmonary bypass  
 AU Takeo, Masahiko  
 CS Med. Sch., Okayama Univ., Okayama, 700, Japan  
 SO Okayama Igakkai Zasshi (1993), 105(1/2), 217-26  
 CODEN: OIZAAV; ISSN: 0030-1558  
 DT Journal  
 LA Japanese  
 CC 1-8 (Pharmacology)  
 AB Mongrel dogs were subjected to 120 min of hypothermic global ischemia by aortic cross clamping with intermittent administration of a cardioplegic solution followed by 60 min reperfusion. They were assigned to 3 groups; group A (no medication before reperfusion), group B (administration of physiol. saline by bolus injection through the aortic root just before reperfusion), and group C [administration of 3 mg/mL/kg MCI-186 (free radical scavenger) in a similar manner to group B]. Cardiac function (left ventricular systolic pressure, cardiac output, left ventricular maximum dP/dt) after 60 min reperfusion expressed as a percent recovery of pre-ischemic state was superior in group C than in groups A and B. Release of lipid peroxide assayed by the TBA method as the difference between coronary artery and sinus were suppressed in the early phase of reperfusion in group C. Myocardial water content after 60 min reperfusion was also less in group C than in groups A and B. These findings suggest that administration of MCI-186 before reperfusion after ischemia is effective in protecting the heart from ischemia-reperfusion injury.  
 ST MCI186 inhibition ischemia heart reperfusion; water heart ischemia inhibition MCI186; lipid peroxide artery ischemia inhibition MCI186  
 IT Cardiovascular agents  
 (MCI-186, myocardial ischemia inhibition by, lipid peroxide of coronary artery in relation to)  
 IT Artery, metabolism  
 (coronary, lipid peroxide metabolism by, ischemia inhibition by MCI-186 in relation to)  
 IT Heart, disease



(ischemia, inhibition of, by MCI-186, lipid peroxide of coronary artery in relation to)

IT Lipids, compounds  
 RL: BIOL (Biological study)  
 (peroxides, of coronary artery, ischemia inhibition by MCI-186 in relation to)

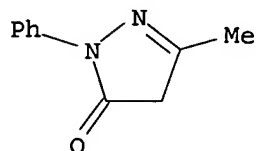
IT Perfusion  
 (re-, heart ischemia in, inhibition of, by MCI-186, lipid peroxide of coronary artery in relation to)

IT 89-25-8, MCI-186  
 RL: BIOL (Biological study)  
 (myocardial ischemia inhibition by, lipid peroxide of coronary artery in relation to)

IT 89-25-8, MCI-186  
 RL: BIOL (Biological study)  
 (myocardial ischemia inhibition by, lipid peroxide of coronary artery in relation to)

RN 89-25-8 HCAPLUS

CN 3H-Pyrazol-3-one, 2,4-dihydro-5-methyl-2-phenyl- (9CI) (CA INDEX NAME)



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L117 ANSWER 1 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2005-384736 [39] WPIX

CR 2003-522788 [49]

DNC C2005-119074

TI Use of agent such as premature vascular senescence ameliorating peroxynitrite scavenger, for treatment of e.g. chronic renal disease, end stage renal disease, systemic lupus erythematosus and Alzheimer's disease.

DC B05

IN CHEN, J; GOLIGORSKY, M S

PA (ARGI-N) ARGINOX INC

CYC 1

PI US 2005113427 A1 20050526 (200539)\* 11 A61K031-41

ADT US 2005113427 A1 Provisional US 2001-329010P 20011012, Cont of US 2002-269032 20021011, US 2004-13457 20041217

PRAI US 2001-329010P 20011012; US 2002-269032

20021011; US 2004-13457 20041217

IC ICM A61K031-41

AB US2005113427 A UPAB: 20050621

NOVELTY - Treatment of an animal with premature vascular senescence, comprises administration of an agent (I) such as premature vascular senescence ameliorating peroxynitrite scavenger or its mixture.

ACTIVITY - Vasotropic; Nootropic; Nephrotropic; Antiinflammatory; Dermatological; Immunosuppressive; Neuroprotective; Antidiabetic.

MECHANISM OF ACTION - None given in the source material.

USE - (I) Is useful for the treatment of an animal (human) with premature vascular senescence, where the animal has elevated levels of advanced glycation end products in blood or tissue, or is affected with a disease such as e.g. end stage renal disease, chronic renal disease, systemic lupus erythematosus or Alzheimer's disease (claimed). (I) Is also useful for the treatment of poorly controlled diabetes, peripheral vascular disease or neurodegenerative diseases.

The ability of (I) to treat end stage renal disease due to glomerulonephritis was tested in humans. The results showed that after administration of (I) (1-20 mg/kg) for thrice/day and 6 months, (I) showed significant subjective improvement of coronary symptoms and renal diseases.

ADVANTAGE - (I) Does not diminish nitric oxide synthesis or activity (claimed) in cell culture in order to forestall adverse effects of reactive oxygen species that tend to appear in cell cultures as a consequence of hypoxic and anoxic episodes.

Dwg.0/1

FS CPI

FA AB; DCN

MC CPI: B04-A06; B04-L03D0E; B05-A03A1; B05-A03A2; B05-B01D; B06-A01; B06-D18; B06-E04; B07-D08; B10-A07A; B10-A17; B10-B02B; B10-C03; B10-E02; B14-E11; B14-F02F3; B14-G02D; B14-J01; B14-N10; B14-N17; B14-S04; B14-S08; B14-S13

TECH UPTX: 20050621

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: (I) Is cystine, cysteine/methionine substituted with tellurium or selenium, polyphenols, flavonoids, plant polyphenols, 3,5-dimethoxy-4-hydroxycinnamic acid (sinapic acid), quercetin, resorufin, bark extracts containing hamamelitannin, phenolic acids, caffeic, chlorogenic and ferulic acids, uric acid, 3-methyl-1-phenyl-2-pyrazolin-5-one, 5,10,15,20-tetrakis(2,4,6-trimethyl-3,5-disulfonatophenyl)-porphyrinato iron (III), 5,10,15,20-tetrakis(N-methyl-4'-pyridyl)-porphyrinato iron (III), 2,3,6-tribromo-4,5-dihydroxybenz methyl ether and/or

2-phenyl-1,2-benzisoselenazol-3(2H)-one.

(I) Is also premature vascular senescence ameliorating peroxy nitrite formation inhibitor that does not diminish nitric oxide synthesis or activity, such as manganese metalloporphyrins, (5,10,15,20-tetrakis(4-carboxyphenyl)-porphyrinato)manganese (III) chloride, manganese (Mn) (III) mesotetrakis (N-ethylpyridinium-2-yl)porphyrin, Mn(II) complex with a bis(cyclohexylpyridine)-substituted macrocyclic ligand, salen-manganese complexes, copper, zinc (Cu,Zn-SOD) that has been genetically engineered to include a positively charged glycine and arginine containing carboxy terminal tail.

ABEX UPTX: 20050621

ADMINISTRATION - Administration of (I) is 0.01 micromol/kg-2 mmol/kg, orally, transdermally, intravenously or intramuscularly.

L117 ANSWER 2 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2005-151096 [16] WPIX

CR 1999-263624 [22]; 2003-585340 [55]; 2003-596829 [56]; 2003-720097 [68]; 2003-730118 [69]; 2003-730119 [69]; 2003-743977 [70]; 2004-010082 [01]; 2004-041182 [04]; 2004-068835 [07]; 2004-339321 [31]; 2004-498809 [47]; 2004-498810 [47]; 2004-552334 [53]; 2004-552335 [53]; 2004-552336 [53]; 2004-552531 [53]; 2005-074026 [08]; 2005-080190 [09]; 2005-141329 [15]; 2005-151097 [16]; 2005-151098 [16]; 2005-171345 [18]; 2005-171346 [18]

DNN N2005-127461 DNC C2005-048733

TI Composition for transmucosal administration of a pharmacologically active compound comprises an active compound, either polar or non-polar solvent and propellant.

DC A17 A25 A96 B04 C07 D16 P34

IN DUGGER, H A

PA (NOVA-N) NOVADEL PHARMA INC

CYC 1

PI US 2005025713 A1 20050203 (200516)\* 14 A61L009-04

ADT US 2005025713 A1 CIP of WO 1997-US17899 19971001, CIP of US 2000-537118 20000329, Div ex US 2002-230075 20020829, US 2004-928979 20040827

PRAI US 2002-230075 20020829; WO 1997-US17899 19971001; US 2000-537118 20000329; US 2004-928979 20040827

IC ICM A61L009-04

AB US2005025713 A UPAB: 20050316

NOVELTY - A buccal spray composition comprising (weight%) either an active compound (a1) (0.1 - 25), polar solvent (10 - 97) and propellant (b1) (2 - 10) of 3-8C hydrocarbon of linear or branched configuration; or (a1) (0.01 - 50, preferably 0.01 - 40, especially 0.05 - 50), non-polar solvent (19 - 89, preferably 25 - 89)) and (b1) (5 - 80, preferably 10 - 70), is new.

DETAILED DESCRIPTION - A buccal spray composition comprises (weight%) either an active compound (a1) (0.1 - 25); polar solvent (10 - 97) and propellant (b1) (2 - 10) of 3-8C hydrocarbon of linear or branched configuration; or (a1) (0.01 - 50, preferably 0.01 - 40, especially 0.05 - 50), non-polar solvent (19 - 89, preferably 25 - 89)) and (b1) (5 - 80, preferably 10 - 70). (a1) Is anti-arrhythmics, anti-hypertensives, heart regulators, cardiovascular agents, plaque stabilization agents, vasodilators, anti-anginals, anti-coagulants, anti-hypotensives, anti-thrombotics, drugs for treating congestive heart failure and/or p-FOX (fatty acid oxidation) inhibitors.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - The composition is useful for transmucosal administration of a pharmacologically active compound (claimed).

ADVANTAGE - The buccal aerosol spray composition provides biologically active compounds for rapid absorption through the oral

mucosa, resulting in fast onset of effect.

Dwg.0/1

FS CPI GMPI

FA AB; DCN

MC CPI: A12-V01; B01-D02; B04-B01C1; B04-C02E1; B04-C03; B04-G21; B04-N04;  
B05-B01E; B06-H; B07-H; B10-A05; B10-A08; B10-A10; B10-A13D; B10-A17;  
B10-A22; B10-B02E; B10-B02F; B10-B03B; B10-C03; B10-C04A; B10-J02;  
B12-M01A; B12-M12A; C01-D02; C04-B01C1; C04-C02E1; C04-C03; C04-G21;  
C04-N04; C05-B01E; C07-H; C10-A05; C10-A08; C10-A10; C10-A13D;  
C10-A17; C10-A22; C10-B02E; C10-B02F; C10-B03B; C10-C03; C10-C04A;  
C10-J02; C12-M01A; C12-M12A; D05-H11A

TECH UPTX: 20050308

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: When the composition comprises polar solvent then the composition additionally comprises a flavoring agent (c1) in an amount of 0.05 - 10 wt.%; and when the composition comprises non-polar solvent then the composition additionally comprises (c1) in an amount of 0.1 - 10 wt.%. The composition comprises (wt.%) either polar solvent (20 - 97, preferably 25 - 97), (a1) (0.1 - 15, preferably 0.2 - 25), (b1) (2 - 5, preferably 2 - 4) and (c1) (0.1 - 5, preferably 0.1 - 2.5); or (b1) (20 - 70), the non-polar solvent (25 - 75), (a1) (0.25 - 35) and (c1) (2 - 7.5).

Preferred Components: The anti-arrhythmic is adenosine, amiodarone, bepridil, bretylium, digitoxin, digoxin, diltiazem, disopyramide, dofetilide, D-sotalol, flecainide, lidocaine, mexiletine, milrinone, phenyloin, pilsicainide, procainamide, propafenone, propranolol, quinidine, tocainide and/or dofetilide. The anti-hypertensive is acebutolol, alfuzosin, amlodipine, atenolol, amlodipine/benazepril, barnidipine benazepril, bepridil, betaxolol, bisoprolol, bosentan, candesartan, captopril, cariporide, carvedilol, celiprolol, cilazapril, clonidine, diltiazem, doxazosin, enalapril, eplerenone, eprosartan, esmolol, felodipine, fenoldopam, fosinopril, guanfacine, imidapril, irbesartan, isradipine, labetalol, lercanidipine, lisinopril, losartan, manidipine, methyldopa, metoprolol, moxonidine, nadolol, nicardipine, nicorandil, nifedipine, nitrendipine, nosoldipine, omapatrilat, perindopril erbumine, pindolol, prazosin, propranolol, quinapril, ramipril, sotalol, spirapril, tamsulosin, telmisartan, terazosin, torsemide, trandolapril, valsartan, vatanidipine and/or midodrine. The heart regulator is digoxin, digitoxin and/or dobutamine. The cardiovascular agent is edaravone, iloprost, levosimendan, molsidomine, tezosentan, tirilazad, YM087, adenosine, avasimibe and/or fenofibrate. The plaque stabilization agent is avasimibe. The vasodilator is buflomedil, cilostazol, dipyridamole, diazoxide, hydralazine, minoxidil, naftidrofuryl, nicorandil, nitroprusside, alprostadil, apomorphine, phentolamine mesylate, sildenafil, tadalafil and/or vardenafil. The anti-anginal is amlodipine, amyl nitrite, atenolol, bepridil, diltiazem, erythrityl tetranitrate, felodipine, isosorbide dinitrate, isradipine, metoprolol, nadolol, nicardipine, nifedipine, nimodipine, pentaerythritol tetranitrate and/or propranolol. The anti-coagulant is abciximab, ardeparin, argatroban, bivalirudin, clopidogrel, dalteparin, danaparoid, desirudin, dipyridamole, enoxaparin, eptifibatide, fondaparinux, H376/95, lepirudin, melagatran, nadroparin, nafamostat mesilate, pentosan, pentoxifylline, reviparin, sarpogrelate, SNAC/SNAD-heparin, ticlopidine, tinzaparin, tirofiban and/or warfarin. The anti-hypotensive is midodrine, dobutamine and/or fludrocortisone. The anti-thrombotic is aspirin, abciximab, enoxaparin, integrilin and/or ticlopidine. The drug for congestive heart failure is amrinone, benazepril, bumetanide, captopril, digitoxin, digoxin, dobutamine, dopamine, enalapril, ethacrynic acid, fosinopril, furosemide, hydralazine, lisinopril, milrinone, minoxidil, moexipril, quinapril, ramipril and/or torsemide. The p-FOX inhibitor is ranolazine.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: (b1) Is propane, N-butane, iso-butane, N-pentane, iso-pentane and/or neo-pentane (preferably n-butane or iso-butane); and has a water content of not more than 0.2% and a concentration of oxidizing agent, reducing agent, Lewis acid and Lewis bases of less than 0.1%. (c1) Is synthetic or natural oil of peppermint, oil of spearmint, citrus oil, fruit flavors and/or sweeteners. The polar solvent is polyethylene glycol having a molecular weight of 400 - 1000, 2-8C mono- - poly-alcohols or 7-18C alcohols of linear or branched configuration (preferably aqueous polyethylene glycol, and aqueous ethanol). The non-polar solvent is 2-24C fatty acid (2-6C) esters, 7-18C hydrocarbons of linear or branched configuration, 2-6C alkanoyl esters or triglycerides of 2-6C carboxylic acids (preferably miglyol).

ABEX UPTX: 20050308

ADMINISTRATION - The composition is administered in the oral mucosa of the mammal by spraying; and also transmucosally (claimed).

EXAMPLE - A polar solvent formulation comprising (weight%) glyburide (0.6 - 10), ethanol (70 - 97), water (0.2 - 2), flavors (0.1 - 2.5) and propellant (3 - 4).

L117 ANSWER 3 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-547652 [53] WPIX

DNC C2004-201015

TI Iron chelating agent useful in pharmaceuticals for protecting tissues against iron deficiency and preventing and treating hyperferremia, contains pyrazolone derivative as active ingredient.

DC B03

PA (YOSH) YOSHITOMI PHARM IND KK

CYC 1

PI JP 2004203820 A 20040722 (200453)\* 16 C07D231-26

ADT JP 2004203820 A JP 2002-376668 20021226

PRAI JP 2002-376668 20021226

IC ICM C07D231-26

ICS A61K031-4152; A61P003-10; A61P009-10; A61P043-00

AB JP2004203820 A UPAB: 20040818

NOVELTY - An iron chelating agent containing pyrazolone derivative (I) as active ingredient, is new.

DETAILED DESCRIPTION - An iron chelating agent contains pyrazolone derivative of formula (I), its salt, hydrate or solvate as active ingredient.

R1 = H, aryl, 1-5C alkyl or 3-6C alkoxyalkyl;

R2 = H, aryloxy, arylmercapto, 1-5C alkyl or 1-3C hydroxyalkyl; or

R1+R2 = 3-5C alkylene; and

R3 = H, 1-5C alkyl, 5-7C cycloalkyl, 1-3C hydroxyalkyl, benzyl, naphthyl, phenyl, 1-5C alkyl, 1-5C alkoxy, 2-5C alkoxyalkyl, 1-3C alkylmercapto, 1-4C alkylamino, 2-8C dialkylamino or phenyl (optionally substituted by 1-3 acetamido, halogen, trifluoromethyl, carboxyl, cyano, hydroxyl, nitro and/or amino).

INDEPENDENT CLAIMS are also included for:

(1) 1:6 complexes of iron and (I); and

(2) pharmaceutical for preventing and treating hyperferremia which contains 1:6 iron:(I) complexes as above.

ACTIVITY - Antianemic; Cardiovascular-Gen.; Antiarteriosclerotic; Cerebroprotective; Cardiant; Antidiabetic.

No biological data given.

MECHANISM OF ACTION - Lipid-Peroxidation-Inhibitor.

USE - Useful in pharmaceuticals for preventing and treating hyperferremia and as tissue protecting agent against iron deficiency

(claimed). Also used in preventing circulatory disorders such as arteriosclerosis, cerebral infarction or myocardial infarction, accompanied with diabetes.

ADVANTAGE - The iron chelating agent has high lipophilicity and is effective in depositing iron in tissues.

Dwg.0/7

FS CPI

FA AB; GI; DCN

MC CPI: B05-A03A; B06-H; B07-D08; **B14-F01B; B14-F02D1;**

**B14-F03; B14-F07; B14-L06; B14-N16**

TECH UPTX: 20040818

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Agent: The iron chelating agent contains trivalent iron and pyrazolone derivative (I) in the form of 1:6 complexes.

ABEX UPTX: 20040818

SPECIFIC COMPOUNDS - Use of one pyrazolone derivative (I) is specifically claimed, i.e. **3-methyl-1-phenyl-2-pyrazolin-5-one** of formula (Ia).

ADMINISTRATION - Administered orally or parenterally at dose of 0.1-1000 mg/kg body weight/day, preferably 0.1-10 mg/kg body weight/day in single or divided dose.

EXAMPLE - Ethyl acetoacetate (13.0 g) and phenylhydrazine (10.8 g) were mixed with ethanol (50 ml), refluxed for 3 hours and cooled to precipitate crystals of **3-methyl-1-phenyl-2-pyrazol-5-one (Edaravone)**. The obtained cured crystals were recrystallized with ethanol to obtain colorless crystals of **edaravone** (11.3 g). 0.1 mM transferrin and 0.1 mM **edaravone** were mixed with buffer, giving a complex with excellent absorption spectrum.

L117 ANSWER 4 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-431515 [40] WPIX

DNC C2004-161535

TI Percutaneous absorption formulations such as patches and ointments containing **edaravone** for improving brain function e.g. in stroke, and treating arteriosclerosis, diabetes, and disorders of liver, kidney and gastrointestinal mucus membrane.

DC A96 B03

IN HASHITANI, H; HORIUCHI, T; MORI, J; SHIMADA, S; WAKI, H; YAMA, S

PA (LEAD-N) LEAD CHEM CO LTD

CYC 101

PI WO 2004041270 A1 20040521 (200440)\* JA 24 A61K031-4152

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU  
MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT  
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA  
ZM ZW

AU 2002344454 A1 20040607 (200469) A61K031-4152

ADT WO 2004041270 A1 WO 2002-JP11518 20021105; AU 2002344454 A1

AU 2002-344454 20021105, WO 2002-JP11518 20021105

FDT AU 2002344454 A1 Based on WO 2004041270

PRAI WO 2002-JP11518 20021105

IC ICM A61K031-4152

ICS A61K009-70; A61K047-10; A61K047-30; A61P009-00

AB WO2004041270 A UPAB: 20040624

NOVELTY - A percutaneous absorption formulation contains 0.1-30 weight% of **3-methyl-1-phenyl-2-**

**pyrazolin-5-one (I)** in a base.

ACTIVITY - Cerebroprotective; Hemostatic; Antiarteriosclerotic; Antidiabetic; Nephrotropic; Hepatotropic; Gastrointestinal-Gen.

A percutaneous absorption formulation containing 3 parts (I) in a mixture of sodium polyacrylate, starch acrylate, talc, glycerine, tartaric acid, water, n-methyl-2-pyrrolidone and crotonamiton was applied to skin separated from a rat, and tested for its transmission through the skin into a receiver cell. Transmission was 3.41 micro g/cm<sup>2</sup> in 1 hour, 1.90.34 micro g/cm<sup>2</sup> in 10 hours, and 643.53 micro g/cm<sup>2</sup> in 24 hours.

MECHANISM OF ACTION - None given.

USE - (I) is used to prevent or improve brain function in humans including cerebral disorders such as cerebral infarction and subarachnoid hemorrhage; and prevent and treat arteriosclerosis, diabetes, and disorders of liver, kidney and gastrointestinal mucus membrane. The formulation is a patch or ointment.

ADVANTAGE - Compared with oral administration, treatment is simple. If side effects occur, it is simple to stop the treatment by removing the formulation. A good blood level of the agent can be maintained for a long time, without requiring intravenous administration.

Dwg.0/1

FS CPI

FA AB; DCN

MC CPI: A12-V01; B04-C03; B07-D08; B12-M02B; B12-M02D; B12-M02F; B12-M07; B14-E10; B14-F02D1; B14-F07; B14-F08; B14-N10; B14-N12; B14-N16; B14-S04

TECH UPTX: 20040624

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred formulation: the formulation base is an aqueous base comprising 1-20 wt.% water-soluble polymer, 0.01-20 wt.% crosslinking agent, 10-80 wt.% polyhydric alcohol and 1-80 wt.% water.

ABEX UPTX: 20040624

EXAMPLE - None given.

L117 ANSWER 5 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-382500 [36] WPIX

DNC C2004-143992

TI Pharmaceutical for prevention and/or treatment of myocarditis, contains free radical scavenger as active ingredient.

DC B03

PA (YOSH) YOSHITOMI PHARM IND KK

CYC 1

PI JP 2004137253 A 20040513 (200436)\* 13 A61K045-00

ADT JP 2004137253 A JP 2003-196173 20030714

PRAI JP 2002-205025 20020715

IC ICM A61K045-00

ICS A61K031-4152; A61P009-00; A61P009-02; A61P009-06; A61P017-00; A61P025-02; A61P031-00; A61P031-12; C07D231-20

AB JP2004137253 A UPAB: 20040608

NOVELTY - Pharmaceutical contains free radical scavenger as an active ingredient.

ACTIVITY - Cardiant; Virucide; Antiarrhythmic; Analgesic; Cardiovascular-Gen.; Antiinflammatory; Anticonvulsant; Vasotropic; Cerebroprotective.

Myocarditis model was produced by inoculating Coxsackie B-virus (0.1 ml of 106 TCID<sub>50</sub>/ml) to 3 week old male C3H/He mouse and inducing myocariditis. **Edaravone** was administered intraperitoneally at a dose of 30 mg/kg after myocarditis onset (from 5-th day of inoculation) and before 14-th day (subacute term). Physiological saline was administered intraperitoneally to control group. **Edaravone** effect was evaluated by measuring plasma thio barbitol acid reaction

material, body weight and cardiac weight in virus inoculated group on 9-th day. The survival rate after 14 days of inoculation was measured. The control group showed 20 % survival rate and **edaravone** administered group showed 70 % survival rate after 14 days of inoculation.

MECHANISM OF ACTION - Antioxidant.

No biological given.

USE - For the prevention and/or treatment of myocarditis e.g. infectious myocarditis caused by virus, and treating illness conditions e.g. cardiac failure, arrhythmia, pectoralgia, palpitation, dyspnea, swelling, face pallor, cyanosis, faint seizure, cold feeling of limbs tip, articular pain, muscular pain, eruption and cardiogenic shock resulting from myocarditis (claimed). Also in brain protective agent.

ADVANTAGE - By administering formulation after onset of myocarditis, survival rate is increased.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B07-D08; B14-A02; B14-C01; B14-C03; **B14-F01A**;

**B14-F01B**; B14-J05; B14-J07; B14-K01; B14-N16; B14-S08

TECH UPTX: 20040608

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Compound: The free radical scavengers are pyrazolone derivative of formula (I), its salt, hydrates or solvates.

R1 = H, aryl, 1-5C alkyl or 3-6C alkoxy carbonylalkyl;

R2 = H, aryloxy, aryl mercapto, 1-5C alkyl or 1-3C hydroxyalkyl, or R1 and R2 together form 3-5C alkylene; and

R3 = H, 1-5C alkyl, 5-7C cycloalkyl, 1-3C hydroxyalkyl, benzyl, naphthyl, 1-5C alkoxy, 1-3C hydroxyalkyl, 2-5C alkylcarbonyl, 1-3C alkyl mercapto, 1-4C alkylamino or phenyl optionally substituted with 1-3 substituents selected from 2-8C dialkylamino, halogen, trifluoromethyl, carboxyl, cyano, hydroxyl, nitro, amino, acetamide or 1-5C alkyl.

ABEX UPTX: 20040608

SPECIFIC COMPOUNDS - The pyrazolone derivative (I) is 3-methyl-1-phenyl-2-pyrazoline-5-one (**Edaravone**).

ADMINISTRATION - Administered orally at a dose of 0.1-1000 (0.5-50) mg/kg/day, or parenterally at a dose of 0.01-100 (0.1-10) mg/kg/day, 1-3 times daily.

EXAMPLE - 13 g of ethyl acetoacetate and 10.8 g of phenyl hydrazine were added to 50 ml of ethanol, refluxed with stirring for 3 hours, crystals were precipitated, filtered after cooling the reaction solution, recrystallized from ethanol and 11.3 g of 3-methyl-1-phenyl-2-pyrazoline-5-one (**Edaravone**) was obtained.

L117 ANSWER 6 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-369134 [35] WPIX

DNC C2004-139864

TI Novel cell-damage marker inhibitor contains pyrazoline-5-one derivative as active ingredient, useful for treating cell-damage diseases such as amyotrophic lateral sclerosis.

DC B03

PA (YOSH) YOSHITOMI PHARM IND KK

CYC 1

PI JP 2004137252 A 20040513 (200435)\* 16 A61K031-4152

ADT JP 2004137252 A JP 2003-194681 20030710

PRAI JP 2002-202977 20020711

IC ICM A61K031-4152



ICS A61P025-28; A61P043-00; C07D231-26

AB JP2004137252 A UPAB: 20040603

NOVELTY - A cell-damage marker inhibitor (MI) containing pyrazolone derivative (PD) (I), as an active ingredient, or its salt, hydrates or solvate, is new.

DETAILED DESCRIPTION - A cell-damage marker inhibitor (MI) contains pyrazolone derivative (PD) of formula (I), as an active ingredient, or its salt, hydrates or solvate.

R1 = H, aryl group, 1-5C alkyl group or total 3-6C alkoxy carbonylalkyl group;

R2 = H, aryloxy group, aryl mercapto group, 1-5C alkyl group or 1-3C hydroxyalkyl group; or

R1+R2 = 3-5C alkylene group;

R3 = H, 1-5C alkyl group, 5-7C cycloalkyl group, 1-3C hydroxyalkyl group, benzyl group, naphthyl group, phenyl group, 1-5C alkoxy group, total 2-5C alkoxy carbonyl group, 1-3C alkyl mercapto group, 1-4C alkylamino group, total 2-8C dialkylamino group or phenyl group substituted by substituents such as halogen atom, trifluoromethyl group, carboxyl group, cyano group, hydroxyl group, nitro group, amino group or acetamide group.

INDEPENDENT CLAIMS are also included for the following:

(1) pharmaceutical (P1) comprising PD as an active ingredient, for treating a patient having raised level of cell-damage marker; and

(2) evaluating the cell-damage inhibitory effect of PD, involving measuring 8-OHdG and S-100 beta in the blood serum of a subject administered with PD.

ACTIVITY - CNS-Gen.; Muscular-Gen.; Neuroprotective; Cerebroprotective; Thrombolytic; Tranquilizer; Vulnerary; Hemostatic; Antiarteriosclerotic; Vasotropic.

MECHANISM OF ACTION - Inhibitor of cell-damage marker (claimed).

In vivo analysis of 3-methyl-1-phenyl-2-pyrazolone-5-one (edaravone) in reducing the level of cell-damage marker was carried out as follows: In a patient having brain-embolism disease, edaravone was administered, and in control, edaravone was not administered. The concentration of S-100 beta in the blood serum was measured for 14 days from the day of administration of medicine. The urine sample was collected and the concentration of 8-OHdG was measured. In the edaravone administered patient, S-100 beta was found to be decreased gradually. The result indicated suppression of neuron failure, in the patient.

USE - MI is useful for treating cell-damage such as neuron failure (claimed). P1 is useful for treating cerebrovascular trauma, motor-neuron disease such as amyotrophic lateral sclerosis, cerebral infarction, cerebral thrombosis, brain-embolism disease, cerebral hemorrhage, head trauma, cerebral arteriosclerosis and transient cerebral ischemic attack.

ADVANTAGE - MI enables reduction of cell-damage markers associated with cell-damage disease and thus evaluating the effectiveness of the treatment.

Dwg. 0/3

FS CPI

FA AB; GI; DCN

MC CPI: B04-B04D4; B07-D08; B11-C08; B12-K04E; B14-F02; B14-F02D1; B14-F04; B14-F07; B14-F08; B14-J01; B14-N16; B14-S01

TECH UPTX: 20040603

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Inhibitor: In MI, the marker is S-100beta or 8-OHdG.

ABEX UPTX: 20040603

SPECIFIC COMPOUNDS - Use of 1 compound as PD is specifically claimed, i.e. 3-methyl-1-phenyl-2-

**pyrazoline -5-one.**

ADMINISTRATION - P1 is administered by oral or parenteral route. Dosage for oral administration ranges from 0.1-1000 mg/kg body weight/day (preferably 0.5-50 mg/kg body weight/day), and for parenteral administration ranges from 0.01-100 mg/kg body weight/day (preferably 0.1-10 mg/kg body weight/day).

L117 ANSWER 7 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-344752 [32] WPIX

DNC C2004-131506

TI Pharmaceutical for preventing and/or treating lung failure such as adult-type respiratory distress syndrome or acute lung injury comprises pyrazolone derivative, salts, hydrates or solvates as active ingredient.

DC B03

PA (YOSH) YOSHITOMI PHARM IND KK

CYC 1

PI JP 2004131402 A 20040430 (200432)\* 16 A61K031-4152

ADT JP 2004131402 A JP 2002-295712 20021009

PRAI JP 2002-295712 20021009

IC ICM A61K031-4152

ICS A61P009-12; A61P011-00; A61P031-04; A61P031-06; A61P031-10; A61P031-12; A61P033-00; A61P037-02

AB JP2004131402 A UPAB: 20040520

NOVELTY - Pharmaceutical for preventing and/or treating lung failure comprises pyrazolone derivative (I) or its salts, hydrates or solvates as an active ingredient.

DETAILED DESCRIPTION - Pharmaceutical for preventing and/or treating lung failure comprises pyrazolone derivative of formula (I) or its salts, hydrates or solvates as an active ingredient.

R1 = H, aryl, 1-5C alkyl, or 3-6C alkoxy carbonylalkyl;

R2 = H, aryloxy, arylmercapto, 1-5C alkyl or 1-3C hydroxyalkyl; and

R3 = H, 1-5C alkyl, 5-7C cycloalkyl, 1-3C hydroxyalkyl, benzyl, naphthyl, phenyl (optionally substituted by H, trifluoromethyl, carboxyl, cyano, hydroxyl, nitro, amino or 1-3 acetamide), 2-5C alkoxy carbonyl, 1-3C alkylmercapto, 1-4C alkylamino or 2-8C dialkylamino.

INDEPENDENT CLAIMS are also included for:

(1) agent for suppressing enhancement of lung capillary permeability comprising (I); and

(2) agent for suppressing pulmonary vascular resistance comprising (I).

ACTIVITY - Respiratory-Gen.

MECHANISM OF ACTION - None given.

USE - For preventing and treating lung failure such as adult-type respiratory distress syndrome or acute lung injury (claimed).

ADVANTAGE - The pharmaceutical effectively prevents and treats lung failure such as adult-type respiratory distress syndrome or acute lung injury. The pharmaceutical suppresses oxidant induced type acute lung injury.

Dwg.0/3

FS CPI

FA AB; GI; DCN

MC CPI: B07-D08; B14-F02; B14-K01

TECH UPTX: 20040520

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The pharmaceutical containing pyrazolone derivative is 3-methyl-1-phenyl-2-pyrazoline -5-one.

ABEX UPTX: 20040520

ADMINISTRATION - Administration of (I) is orally at 0.1-1000 (preferably

0.5-50) mg/kg/day or parenterally at 0.01-100 (preferably 0.1-10) mg/kg/day.

L117 ANSWER 8 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-322623 [30] WPIX

DNC C2004-122982

TI Sodium-calcium exchange inhibitor useful in preventing and treating cardiac failure, hypertension and arrhythmias, comprises pyrazolone derivative, its salt, its hydrate or its solvate as active ingredient.

DC B02 B03

PA (YOSH) YOSHITOMI PHARM IND KK

CYC 1

PI JP 2004115511 A 20040415 (200430)\* 12 A61K031-4152

ADT JP 2004115511 A JP 2003-314843 20030905

PRAI JP 2002-261834 20020906

IC ICM A61K031-4152

ICS A61P009-04; A61P009-06; A61P009-10; A61P009-12; A61P043-00; C07D231-26

AB JP2004115511 A UPAB: 20040511

NOVELTY - A sodium-calcium exchange inhibitor comprises pyrazolone derivative (I), its salt, its hydrate or its solvate as active ingredient.

DETAILED DESCRIPTION - The sodium-calcium exchange inhibitor comprises pyrazolone derivative of formula (I), its salt, its hydrate or its solvate as active ingredient.

R1 = hydrogen, aryl, 1-5C alkyl or 3-6C alkoxy carbonyl alkyl group;

R2 = H, aryloxy, aryl mercapto, 1-5C alkyl or 1-3C hydroxyl alkyl group;

R1+R2 = 3-5C alkylene group; and

R3 = H, 1-5C alkyl, 5-7C cycloalkyl, 1-3C hydroxy alkyl, benzyl, naphthyl, phenyl, 1-5C alkoxy, 2-5C alkoxy carbonyl, 1-3C alkyl mercapto, 1-4C alkyl amino or phenyl group substituted by halogen atom, trifluoro methyl group, carboxyl group, cyano group, hydroxyl group, nitro group, amino group or acetamide group.

ACTIVITY - Vasotropic; Cardiant; Hypotensive; Antiarrhythmic. No biological data given.

MECHANISM OF ACTION - Na-Ca-Exchange-Inhibitor. Test details are described but no results are given.

USE - In preventing and treating ischemic heart disease, cardiac failure, hypertension and arrhythmias (claimed).

ADVANTAGE - The sodium-calcium exchange inhibitor has excellent ischemic heart disease, cardiac failure, hypertension and arrhythmias preventing and treating effect, and is highly safe.

Dwg.0/2

FS CPI

FA AB; GI; DCN

MC CPI: B07-D08; B14-F01A; B14-F01B; B14-F01E; B14-F02B; B14-L06

ABEX UPTX: 20040511

SPECIFIC COMPOUNDS - Use of 3-methyl-1-phenyl-2-pyrazoline-5-one as (I) is claimed.

ADMINISTRATION - Administered orally at a dose of 0.1-1000 mg/kg/day, preferably 0.5-50 mg/kg/day in single or divided doses. Administered parenterally at a dose of 0.01-100 mg/kg/day, preferably 0.1-10 mg/kg/day in single or divided doses.

EXAMPLE - Ethyl acetoacetate (in g) (13) and phenyl hydrazine (10.8) was added to ethanol (50 ml), reacted for 3 hours, filtered and recrystallized from ethanol to obtain 3-methyl-1-

**phenyl-2-pyrazoline-5-one**

(11.3) having melting point of 127.5-128.5.

L117 ANSWER 9 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-322620 [30] WPIX

DNC C2004-122979

TI Agent used for preventing and/or treating arterial wall failure caused by percutaneous transluminal coronary angioplasty, contains pyrazolone derivatives.

DC B03

IN **MORI, T; TANAKA, T**

PA (YOSH) YOSHITOMI PHARM IND KK; (MORI-I) MORI T; (TANA-I) TANAKA T

CYC 2

PI JP 2004115505 A 20040415 (200430)\* 12 A61K031-4152

US 2004254234 A1 20041216 (200482) A61K031-4152 &lt;--

ADT JP 2004115505 A JP 2003-311057 20030903; US 2004254234 A1 US

**2003-643404 20030818**PRAI **JP 2002-258503 20020904**

IC ICM A61K031-4152

ICS A61P009-10; C07D231-22

AB JP2004115505 A UPAB: 20040511

NOVELTY - Agent contains pyrazolone derivatives (I).

DETAILED DESCRIPTION - Agent contains pyrazolone derivatives of formula (I), their salts, hydrates or solvates.

R1 = H, aryl, 1-5C alkyl or 3-6C alkoxyalkyl;

R2 = H, aryloxy, arylmercapto, 1-5C alkyl or 1-3C hydroxyalkyl or

R1 + R2 = 3-5C alkylene, and

R3 = H, 1-5C alkyl, 5-7C cycloalkyl, 1-3C hydroxyalkyl, benzyl, naphthyl, 1-5C alkyl, 1-5C alkoxy, 1-3C hydroxyalkyl, 2-5C alkoxyalkyl, 1-3C alkylmercapto, 1-4C alkylamino, 2-8C dialkylamino or phenyl (optionally substituted by 1-3 halo, trifluoromethyl, carboxy, cyano, hydroxy, nitro, amino or acetamide).

ACTIVITY - Cardiant; Vasotropic.

Japanese white rabbits were divided into an **edaravone** group and control group each containing 6 animals. 1% cholesterol food was fed to the animals for 10 weeks. Abdominal aorta failure occurred at the 8th week. 10 mg/kg of **edaravone** was administered intravenously twice a day to the **edaravone** group and physiological saline to the control group daily. After 10 weeks, the animals were killed and the abdominal aorta was extracted. The ratio between the new inner membrane and inside membrane was measured by hematoxylin eosin staining. Blood serum total cholesterol, neutral fat and peroxylipid were measured before administering cholesterol food and before killing the animal, when the failure occurred. The results showed that the **edaravone** administered group suppressed hypertrophy due to the new inner membrane, compared to the control group.

MECHANISM OF ACTION - None given.

USE - Used as antioxidant agent for the prevention and/or treatment of arterial wall failure caused by percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass graft (CABG) (claimed), cerebral blood vessel and peripheral artery failure. The arterial wall failure is restenosis and new inner membrane hypertrophy after PTCA or CABG.

ADVANTAGE - (I) Protect the brain, have high reactivity to active oxygen and prevent cell damage.

Dwg.0/3

FS CPI

FA AB; GI; DCN

MC CPI: B07-D08; **B14-F01; B14-F02**

TECH UPTX: 20040511

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Compounds: (I) comprises **3-methyl-1-phenyl-2-pyrazoline-5-one (Ia)**.

ABEX UPTX: 20040511

ADMINISTRATION - Administered orally at a dose of 0.1-1000 (preferably 0.5-50) mg/kg/day or parenterally at a dose of 0.01-100 (preferably 0.1-10) mg/kg/day, 1-3 times daily.

EXAMPLE - None given.

L117 ANSWER 10 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-299618 [28] WPIX

DNC C2004-114929

TI Percutaneous and/or transmucous absorption external preparation e.g. lotion for treating diseases caused by free radical such as inflammation, contains **3-methyl-1-phenyl-2-pyrazoline-5-one** and/or its salt as active ingredient.

DC B03 B07

PA (MIKA) MIKASA SEIYAKU KK

CYC 1

PI JP 2004099486 A 20040402 (200428)\* 9 A61K031-4152

ADT JP 2004099486 A JP 2002-261495 20020906

PRAI JP 2002-261495 20020906

IC ICM A61K031-4152

ICS A61K009-127; A61K009-52; A61P001-04; A61P001-16; A61P001-18; **A61P003-00; A61P003-10; A61P005-00; A61P007-00;**  
A61P009-06; A61P009-10; A61P011-00; A61P013-12; A61P019-02;  
A61P025-16; A61P025-34; A61P027-12; A61P029-00; A61P031-00;  
A61P031-04; A61P035-02; A61P037-08; A61P039-06; A61P043-00;  
C07D231-26

AB JP2004099486 A UPAB: 20040429

NOVELTY - Percutaneous and/or transmucous absorption external preparation for treating diseases caused by free radical contains **3-methyl-1-phenyl-2-pyrazoline-5-one** and/or its salt as an active ingredient.

ACTIVITY - Antiinflammatory; Cytostatic; Antibacterial; Immunosuppressive; Cardiovascular-Gen.; Cerebroprotective; Cardiant; Vasotropic; Antiparkinsonian; Antiarrhythmic; Antiartherosclerotic; Gastrointestinal-Gen.; Respiratory-Gen.; Hepatotropic; Ophthalmological; Endocrine-Gen.; Nephrotropic; Antidiabetic; Tranquilizer; Antiulcer; Antirheumatic; Antiarthritic; Antiallergic.

MECHANISM OF ACTION - Antioxidant.

USE - As powder, suspension, lotion, ointment, cream, gel, poultice, plaster, patch, etc., for preventing or treating inflammation, cell, cytoplasmic membrane failure, leukemia, sepsis, cardiovascular system lesions, cerebral edema, cerebral infarction, cerebral hemorrhage, Parkinson's disease, myocardial infarction, arrhythmia, arteriosclerosis, gastrointestinal disorders, respiratory diseases, pneumonia, gastric-mucosa failure, liver cirrhosis, pancreatic inflammation, autoimmune diseases, ophthalmologic disease, endocrine system disease, renal disease, glomerulonephritis, hemolytic renal disease, diabetes, stress reaction, cataract, corneal ulcer, atopic disease, rheumatoid arthritis and allergy.

ADVANTAGE - **3-methyl-1-phenyl-2-pyrazoline-5-one** is safe and the external preparation has excellent bioavailability since the compound is effectively absorbed through skin, nose, lungs and oral cavity.

Dwg.0/2

FS CPI

FA AB; DCN  
 MC CPI: B07-D08; B12-M02; B12-M11G; B14-A01; B14-C03; B14-C09B; B14-E10;  
**B14-F01; B14-F01A; B14-F07;**  
**B14-F08;** B14-G02A; B14-G02D; B14-H01A; B14-J01A3; B14-K01;  
 B14-N03; B14-N10; B14-N12; B14-N13; B14-N17C; B14-S04; B14-S08  
 TECH UPTX: 20040429  
 TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The active ingredient is in the form of liposome and micro or nano sphere. Preferred Composition: The external preparation contains 0.01-80 weight/weight% of **3-methyl-1-phenyl-2-pyrazoline-5-one.**

L117 ANSWER 11 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-288987 [27] WPIX

DNC C2004-111142

TI Oral formulation for preventing and treating cerebrovascular accidents, comprises pyrazolone derivative, its salt, its hydrate or its solvate as active ingredient, and has specific pharmacokinetic properties.

DC B03

PA (YOSH) YOSHITOMI PHARM IND KK

CYC 1

PI JP 2004091441 A 20040325 (200427)\* 13 A61K031-4152

ADT JP 2004091441 A JP 2002-258502 20020904

PRAI JP 2002-258502 20020904

IC ICM A61K031-4152

ICS A61P039-06; C07D231-26

AB JP2004091441 A UPAB: 20040426

NOVELTY - An oral formulation comprises pyrazolone derivative (I), its salt, its hydrate or its solvate as active ingredient. The compound has maximum blood concentration (cmax) and maximum concentration attainment time (tmax) of 174-15000 ng/ml and 0.1-1 hour, respectively.

DETAILED DESCRIPTION - The oral formulation comprises pyrazolone derivative of formula (I), its salt, its hydrate or its solvate as active ingredient. The compound has maximum blood concentration (cmax) and maximum concentration attainment time (tmax) of 174-15000 ng/ml and 0.1-1 hour, respectively.

R1 = hydrogen, aryl group, 1-5C alkyl group or 3-6C alkoxy carbonyl alkyl group;

R2 = H, aryloxy group, aryl mercapto group, 1-5C alkyl group or 1-3C hydroxy alkyl group;

R1+R2 = 3-5C alkylene group;

R3 = H, 1-5C alkyl group, 5-7C cycloalkyl group, 1-3C hydroxyalkyl group, benzyl group, naphthyl group, 1-5C alkoxy group, 2-5C alkoxy carbonyl group, 1-3C alkyl mercapto group, 1-4C alkyl amino group, 2-8C dialkyl amino group or phenyl group substituted with halogen, tri fluoromethyl, carboxyl, cyano, hydroxyl, nitro or amino group.

ACTIVITY - Cerebroprotective; Vasotropic; Antiinflammatory; Vulnerary; Cardiant; Antiulcer; Ophthalmological. No biological data given.

MECHANISM OF ACTION - Antioxidant. No biological data given.

USE - For preventing and treating diseases related to free radicals (claimed) such as ischemic cerebrovascular accidents, cerebral edema due to cerebral infarction, brain embolism, intracerebral hemorrhage, cerebral arteriosclerosis, head trauma, myocardial infarction, spinal injury, gastric ulcer and cataract.

ADVANTAGE - The oral formulation has excellent oral absorptivity and free radical eliminating effect.

DESCRIPTION OF DRAWING(S) - The graph shows the relationship between time and blood concentration of **edaravone (3-methyl-1-phenyl-2-pyrazoline**

-5-one) with respect to rat. (Drawing includes non-English language text).

Dwg.1/1

FS CPI

FA AB; GI; DCN

MC CPI: B07-D08; B14-E08; B14-F01B; B14-F02D;  
B14-F07; B14-F08; B14-N03; B14-N16; B14-S08

TECH UPTX: 20040426

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Properties: After administering 10 mg/kg of the pyrazolone derivative to rats, the concentration of pyrazolone derivative in blood initially, after 15 minutes, and after 1 hour of administration are 10-20 ng/ml, 100-400 ng/ml and 40-80 ng/ml, respectively. After administering 30 mg/kg of pyrazolone derivative, the concentration of pyrazolone derivative in blood initially, after 15 minutes, and after 1 hour of administration are 15-30 ng/ml, 500-2000 ng/ml and 100-400 ng/ml, respectively.

ABEX UPTX: 20040426

SPECIFIC COMPOUNDS - Use of 3-methyl-1-phenyl-2-pyrazoline-5-one is specifically claimed.

ADMINISTRATION - Administered orally at a dose of 10-100 mg/kg (stat dose) with respect to rats (claimed). Administered orally at dose of 0.1-1000 mg/kg, preferably 0.5-50 mg/kg in single or divided doses.

EXAMPLE - Ethyl acetoacetate (in g) (13) and phenyl hydrazine (10.8) were added to ethanol (50 ml) and stirred for 3 hours. The precipitated crystals were filtered and recrystallized from ethanol to obtain 3-methyl-1-phenyl-2-

pyrazoline-5-one (11.3) having melting point 127.5-128.5degreesC. The compound exhibited excellent oral absorptivity when evaluated in 8-week-old Wistar male rats.

L117 ANSWER 12 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-195325 [19] WPIX

DNC C2004-078156

TI Pharmaceutical for brain protection, cerebral function normalization and perform mild hypothermia medical treatment, contains pyrazolone derivative, as active ingredient.

DC B03 B04 D16

PA (YOSH) YOSHITOMI PHARM IND KK

CYC 1

PI JP 2004002400 A 20040108 (200419)\* 13 A61K031-4152

ADT JP 2004002400 A JP 2003-116575 20030422

PRAI JP 2002-120334 20020423

IC ICM A61K031-4152

ICS A61P007-10; A61P009-00; A61P009-10; A61P017-02; A61P025-00;  
A61P025-28; A61P039-06; C07D231-26

AB JP2004002400 A UPAB: 20040318

NOVELTY - A pharmaceutical contains pyrazolone derivative (I), its salts, hydrates or solvates, as an active ingredient.

DETAILED DESCRIPTION - A pharmaceutical contains pyrazolone derivative of formula (I), its salts, hydrates or solvates as an active ingredient.

R1 = H, aryl, 1-5C alkyl or 3-6C alkoxy carbonylalkyl;

R2 = H, aryloxy, aryl mercapto, 1-5C alkyl or 1-3C hydroxyalkyl;

R1, R2 = together form 3-5C alkylene; and

R3 = H, 1-5C alkyl, 5-7C cycloalkyl or 1-3C hydroxyalkyl, benzyl, naphthyl, 1-5C alkoxy, 2-5C alkoxy carbonyl, 1-3C alkyl mercapto, 1-4C alkylamino, 2-8C dialkylamino, phenyl substituted by halo,

trifluoromethyl, carboxyl, cyano, hydroxyl, nitro or amino.

ACTIVITY - Cerebroprotective; Nootropic; Tranquilizer; Vasotropic; Hemostatic; Anticoagulant; Thrombolytic; Vulnerary; Antiinflammatory.

Cerebral ischemia was induced in Sprague Dawley rat with body weight of 200-250 g. A group-III administered with **edaravone** at a dose of 3 mg/kg and simultaneously subjected to hypothermia (35 deg. C) medical treatment, showed excellent reduction in cortex infarction and striate-body infarction volume compared to vehicle administered to group-I.

MECHANISM OF ACTION - None Given.

USE - For the protection of brain and/or normalization of cerebral function, and to perform mild hypothermia medical treatment. Also for the prevention of recurrence of cerebral disorder, cognitive impairment during acute or chronic cerebrovascular accident and anesthesia recovery, improvement of neuroses, cerebral infarction, stroke, intracerebral hemorrhage, cerebral thrombosis, brain embolism, head trauma, ischemic cerebrovascular accident, cerebral edema, subacute cerebrovascular accident after prolongation of life, vascular dementia and cerebrovascular tissue lesion accompanied by aging. (All claimed.)

ADVANTAGE - The pharmaceutical effectively maintains cerebral temperature at 34-36 deg. C, increases effectiveness rate of mild hypothermia medical treatment, reduces serious side effects and mortality rate.

DESCRIPTION OF DRAWING(S) - The drawing shows the measurement result of cortex infarction volume and striate-body infarction volume in each test rat. (Drawing contains non-English language text).

Dwg.1/3

FS CPI

FA AB; GI; DCN

MC CPI: B07-D08; B14-C05; **B14-F02D1**; **B14-F04**;  
**B14-F08**; B14-J01A4; B14-J01B4; B14-N16; B14-N17B; D05-C;  
D05-H08

ABEX UPTX: 20040318

SPECIFIC COMPOUNDS - One compound (I) is claimed, i.e. 3-methyl-1-phenyl-2-pyrazoline-5-one (Ia).

ADMINISTRATION - Administered orally at a dose of 0.1-1000 (0.5-50) mg/kg/day. Administered parenterally a dose of 0.01-100 (0.1-10) mg/kg/day, once or two times daily.

EXAMPLE - 13 g of ethyl acetoacetate and 10.8 g of phenylhydrazine were added to 50 ml of ethanol, refluxed, stirred for 3 hours, crystal precipitate was filtered after cooling the reaction solution, recrystallized from ethanol, and 11.3 g of 3-methyl-1-phenyl-2-pyrazoline-5-one (**edaravone**) colorless crystals were obtained with an yield of 67 %. **Edaravone** had melting point of 127.5-128.5.

L117 ANSWER 13 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-082088 [08] WPIX

DNC C2004-033826

TI Agents for treating and preventing ischemic hepatic reperfusion injury e.g. after liver transplantation comprise pyrazole derivatives.

DC B03

IN NINOMIYA, M; SHIMADA, M

PA (MITS-N) MITSUBISHI PHARMA CORP

CYC 102

PI WO 2003105909 A1 20031224 (200408)\* JA 30 A61K031-4152

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS



LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW  
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ  
 LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT  
 RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA  
 ZM ZW

AU 2003242320 A1 20031231 (200451) A61P001-16

ADT WO 2003105909 A1 WO 2003-JP7477 20030612; AU 2003242320 A1 AU 2003-242320  
 20030612

FDT AU 2003242320 A1 Based on WO 2003105909

PRAI JP 2002-172172 20020613

IC ICM A61K031-4152; A61P001-16

ICS A61K031-516; A61P009-10; C07D231-20; C07D231-22; C07D231-56

AB WO2003105909 A UPAB: 20040202

NOVELTY - Agents for treating and preventing ischemic hepatic reperfusion injury comprise a pyrazole derivative (I).

DETAILED DESCRIPTION - Agents for treating and preventing ischemic hepatic reperfusion injury comprise a pyrazole derivative of formula (I) or its salt, hydrate and/or solvate.

R1 = H, Alk or 3-6C alkoxyacetyl;

Alk = 1-5C alkyl;

R2 = H, aryloxy, arylthio, Alk or 1-3C hydroxyalkyl; or

R1+R2 = 3-5C alkylene;

R3 = H, Alk, 5-7C cycloalkyl, 1-3C hydroxyalkyl, benzyl, naphthyl or phenyl (optionally substituted by 1-3 Alk, OAlk, 1-3C hydroxyalkyl, 2-5C alkoxyacetyl, 1-3C alkylthio, 1-4C alkylamino, 2-8C dialkylamino, halo, CF3, COOH, CN, OH, NO2, NH2 or acetamido).

An INDEPENDENT CLAIM is also included for an agent for protecting a transplanted liver comprising (I).

ACTIVITY - Hepatotropic; Vasotropic.

In an hepatic ischemia model on livers from Wistar rats addition of **edaravone** at 10 mg/l to preservation solution reduced malonic dialdehyde concentration 120 minutes after transplantation from 97.4 nmol/l/g for a control to 29.7 nmol/l/g.

MECHANISM OF ACTION - None given.

USE - For treating and preventing ischemic hepatic reperfusion injury especially after liver transplantation.

Dwg.0/2

FS CPI

FA AB; GI; DCN

MC CPI: B06-H; B07-D08; **B14-F02D**; B14-N10

ABEX UPTX: 20040202

SPECIFIC COMPOUNDS - 1 Compound (I) is specifically claimed, i.e. **3-methyl-1-phenyl-2-pyrazoline-5-one** (Ia).

ADMINISTRATION - Administration of (I) is 0.1-1000 (preferably 0.5-50) mg/kg/day orally or 0.01-100 (preferably 0.1-10) mg/kg/day parenterally.

L117 ANSWER 14 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-065665 [07] WPIX

DNC C2004-027595

TI Agent containing pyrazolinone compound useful for repairing fibrotic tissue lesions in disorders such as keloidosis, ischemia, arteriosclerosis, and hepatic, pulmonary and renal fibrosis, and in cosmetics to treat wrinkles.

DC B03 D21

PA (AJIN) AJINOMOTO KK

CYC 1

PI JP 2003335671 A 20031125 (200407)\* 14 A61K031-4152

ADT JP 2003335671 A JP 2002-144719 20020520

PRAI JP 2002-144719 20020520

IC ICM A61K031-4152

ICS A61K007-00; A61K007-48; A61P001-16; A61P009-08; A61P009-10;  
A61P011-00; A61P013-08; A61P013-12; A61P017-02; A61P037-00;  
A61P043-00; C07D231-20; C07D231-22; C07D231-26; C07D231-38

AB JP2003335671 A UPAB: 20040128

NOVELTY - An agent to repair fibrotic tissue lesions contains an N-substituted pyrazolinone derivative (I) or its salt.

DETAILED DESCRIPTION - An agent to repair fibrotic tissue lesions contains an N-substituted pyrazolinone derivative of formula (I) or its salt.

R1 = H, lower alkyl (optionally substituted by A' or substituted aryl), lower alkenyl (optionally substituted by A'), lower alkynyl (optionally substituted by A'), cycloalkyl, heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, lower alkylcarbonyl, arylcarbonyl, or heteroarylcarbonyl;

A' = hydroxy, halo, alkoxy, aryloxy, heteroaryloxy, mercapto, alkylthio, arylthio, heteroarylthio, cycloalkyl, heterocyclyl, aryl, heteroaryl, or optionally substituted amino;

R2, R3 = H, lower alkyl (optionally substituted by A'), lower alkenyl (optionally substituted by A'), lower alkynyl (optionally substituted by A'), cycloalkyl, heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, lower alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, lower alkylthio, lower alkenylthio, lower alkynylthio, arylthio, heteroarylthio, lower alkoxy, aryloxy or heteroaryloxy;

R4 = lower alkyl (optionally substituted by A'), lower alkenyl (optionally substituted by A'), lower alkynyl (optionally substituted by A'), cycloalkyl, heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, lower alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, lower alkylthio, lower alkenylthio, lower alkynylthio, arylthio, heteroarylthio, lower alkoxy, aryloxy, heteroaryloxy, carboxy, lower alkoxycarbonyl, lower alkenyloxycarbonyl, lower alkynyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, optionally substituted amino, optionally substituted carbamoyl, optionally substituted sulfamoyl, imino, urea, or thiourea.

ACTIVITY - Antiarteriosclerotic; Cardiant; Cytostatic; Hepatotropic; Keratolytic; Nephrotropic; Respiratory-Gen.; Vasotropic.

The amount of fibrous collagen accumulated in human fibroblasts (HFL-1) was determined when cultured with varying concentrations of 14 test compounds (I). Concentrations of 1-methyl-3-(4-methylphenyl)-pyrazolin-5-one inhibited accumulation with IC60 of 150 micro M, compared with IC60 of more than 1 mM for the comparison compound 5-methyl-1-phenyl-2-(1H)-pyridone.

MECHANISM OF ACTION - None given.

USE - The agent is used in compositions to prevent or treat disease produced by accumulation of extra-cellular matrix, liver cirrhosis, hepatic fibrosis, pulmonary fibrosis, kidney fibrosis, cardiac fibrosis, postoperative accretion, arteriosclerosis, nephrosclerosis, systemic sclerosis disease, prostatic hypertrophy, keloidosis, myocardosis, collagen disease, scarring (cicatix), ischemia, or respiratory insufficiency; and in cosmetics to prevent or treat wrinkles (claimed) in humans or animals. The cosmetic is e.g. makeup, skin-care product, lotion, cream, toilet water, pack, washing material, lipstick, foundation, or scalp cosmetic.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B06-H; B07-D08; B14-F02D; B14-F07; B14-K01;

B14-N07A; B14-N10; B14-N12; B14-N17; B14-R01; B14-R02; D08-B03;

D08-B09A1

ABEX

UPTX: 20040128

SPECIFIC COMPOUNDS - Use of 14 compounds (I) is specifically claimed, e.g. 3-methyl-1-phenyl-pyrazolin-5-one (Ia).

ADMINISTRATION - Dosage is 0.001 to 10000 mg/kg/day orally. It may also be given parenterally.

DEFINITIONS - Preferred definitions:

R1 = optionally substituted aryl, optionally substituted heteroaryl, lower alkyl carbonyl, aryl carbonyl, heteroaryl carbonyl, lower alkyl, or lower alkenyl;

R2, R3 = H, lower alkyl carbonyl, aryl carbonyl, or heteroaryl carbonyl;

R4 = lower alkyl, optionally substituted amino, lower alkoxy carbonyl, lower haloalkyl, optionally substituted heteroaryl or optionally substituted aryl.

L117 ANSWER 15 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-039672 [04] WPIX

DNC C2004-015976

TI Novel nitrogen monoxide radical remover for treatment of disease resulting from nitrogen monoxide radical, contains pyrazolone derivative, as active ingredient.

DC B03

PA (YOSH) YOSHITOMI PHARM IND KK

CYC 1

PI JP 2003342173 A 20031203 (200404)\* 8 A61K031-4152

ADT JP 2003342173 A JP 2003-77304 20030320

PRAI JP 2002-78189 20020320

IC ICM A61K031-4152

ICS A61P009-00; A61P025-00; A61P037-02; A61P039-06; C07D231-26

AB JP2003342173 A UPAB: 20040115

NOVELTY - A novel nitrogen monoxide radical remover contains specific pyrazolone derivative (I) or its physiologically acceptable salt, its hydrates or solvate, as the active ingredient.

DETAILED DESCRIPTION - A novel nitrogen monoxide radical remover contains pyrazolone derivative of formula (I) or its physiologically acceptable salt, its hydrates or solvate, as the active ingredient.

R1 = H, aryl, 1-5C alkyl or 3-6C alkoxy carbonyl alkyl;

R2 = H, aryloxy, arylmercapto, 1-5C alkyl or 1-3C hydroxy alkyl, R1 and R2 jointly express 3-5C alkylene; and

R3 = H, 1-5C alkyl, 5-7C cycloalkyl, 1-3C hydroxyalkyl, benzyl, naphthyl, phenyl, 1-5C alkoxy, 1-3C hydroxy alkyl, 2-5C alkoxy carbonyl, 1-3C alkyl mercapto, 1-4C alkyl amino, 2-8C dialkyl amino, phenyl substituted by halogen atom, trifluoro methyl, carboxyl, cyano, hydroxyl group, nitro, amino and substituent chosen from group containing acetamide.

ACTIVITY - Antidote.

MECHANISM OF ACTION - None given.

USE - (I) Are used for the prevention and treatment of disease resulting from nitrogen monoxide radical, and medical agent of vascular system, nervous system and immune system.

ADVANTAGE - The nitrogen monoxide radical remover, is effectively used in the field of pharmaceuticals.

Dwg.0/4

FS CPI

FA AB; GI; DCN

MC CPI: B06-D05; B07-D08; B14-F02; B14-G01; B14-G02; B14-G03;

B14-J01; B14-M01

ABEX

UPTX: 20040115

SPECIFIC COMPOUNDS - The use of one compound (I) is claimed, i.e.

**3-methyl-1-phenyl-2-pyrazoline-5-one.**

L117 ANSWER 16 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-002977 [01] WPIX

DNC C2004-001375

TI Apoptosis inhibitor for preventing and treating diseases resulting from apoptosis promotion, such as autoimmune diseases and neurodegenerative diseases, comprises pyrazolone derivative or its salt as active ingredient.

DC B03

PA (YOSH) YOSHITOMI PHARM IND KK

CYC 1

PI JP 2003300880 A 20031021 (200401)\* 7 A61K031-4152

ADT JP 2003300880 A JP 2003-30644 20030207

PRAI JP 2002-33073 20020208

IC ICM A61K031-4152

ICS A61P009-10; A61P025-28; A61P037-02; A61P043-00; C07D231-20

AB JP2003300880 A UPAB: 20040102

NOVELTY - Novel apoptosis inhibitor comprises pyrazolone derivative (I) or its salt as active ingredient.

DETAILED DESCRIPTION - The new apoptosis inhibitor comprises pyrazolone derivative having formula (I) or its salt as active ingredient.

R1 = H, aryl, 1-5C alkyl or 3-6C alkoxy carbonyl alkyl; and

R2 = H, aryloxy, arylmercapto, 1-5C alkyl or 1-3C hydroxyalkyl; or

R1+R2 = 3-5C alkylene; and

R3 = phenyl (optionally substituted with 1-5C alkyl, 5-7C cycloalkyl, 1-3C hydroxyalkyl, benzyl, naphthyl, phenyl, 1-5C alkoxy, 2-5C alkoxy carbonyl, 1-3C alkylmercapto, 1-4C alkyl amino, 2-8C dialkyl amino, trifluoro methyl, halogen atom, cyano, carboxyl, nitro, amino and/or acetamide.

An INDEPENDENT CLAIM is also included for agent used in preventing and treating diseases resulting from apoptosis promotion, containing the pyrazolone derivative (I) or its salt.

ACTIVITY - Immunosuppressive; Neuroprotective; Nootropic; Vasotropic. No biological data given.

MECHANISM OF ACTION - Apoptosis-Inhibitor. Ischemia induced rabbits were transvenously administered with 3 mg/kg of 1-phenyl-3-methyl-2-pyrazoline-5-one and 30000 Units/kg of super oxide dismutase. The apoptosis induction in rabbits was evaluated using fluorescent-labeled DNA dUTP by TUNEL method. A control was performed without administering the pyrazolone derivative. The apoptosis induction of the test and control was 1-2% and 8-9%, respectively. The results concluded that the test exhibited excellent apoptosis inhibiting than the control.

USE - For preventing and treating diseases resulting from apoptosis promotion (claimed); such as autoimmune diseases, neurodegenerative diseases, ischemic diseases.

DESCRIPTION OF DRAWING(S) - The graph shows the apoptosis induction (%) in test (pyrazolone derivative administration group) and control.

Dwg.1/2

FS CPI

FA AB; GI; DCN

MC CPI: B06-D05; B07-D08; B14-F02D; B14-G02D; B14-H04; B14-J01

ABEX UPTX: 20040102

SPECIFIC COMPOUNDS - 1-Phenyl-3-methyl-2-pyrazoline-5-one (Ia) is specifically claimed as (I).

EXAMPLE - Ethyl acetate (in g) (30), phenyl hydrazine (10.8) and ethanol (50 ml) were reacted for 3 hours. Then the obtained crystals were filtered, cooled and recrystallized from ethanol to obtain

1-phenyl-3-methyl-2-pyrazoline-5-one (11.3) having melting point of 127.5-128.5.

L117 ANSWER 17 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN  
 AN 2003-845201 [78] WPIX  
 DNC C2003-237489  
 TI Agent for treating myocardial disease, especially damage associated with diabetes, contains pyrazolinone derivative.  
 DC B03  
 IN HAYASHI, T  
 PA (MITS-N) MITSUBISHI PHARMA CORP  
 CYC 102  
 PI WO 2003080583 A1 20031002 (200378)\* JA 28 C07D231-20  
 RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS  
 LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW  
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ  
 LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT  
 RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA  
 ZM ZW  
 AU 2003227257 A1 20031008 (200432) C07D231-20  
 ADT WO 2003080583 A1 WO 2003-JP3813 20030327; AU 2003227257 A1 AU 2003-227257  
 20030327  
 FDT AU 2003227257 A1 Based on WO 2003080583  
 PRAI JP 2002-87499 20020327  
 IC ICM C07D231-20  
 ICS A61K031-4152; A61P009-00; A61P009-04; C07C231-22  
 AB WO2003080583 A UPAB: 20031203  
 NOVELTY - Agent for treating myocardial disease contains a pyrazolin-5-one (I), its derivative, or its salts.  
 DETAILED DESCRIPTION - Agent for treating myocardial disease contains a pyrazolin-5-one compound of formula (I), its derivative, or its salts.  
 R1 = H, aryl, 1-5C alkyl or 3-6C alkoxy-carbonylalkyl;  
 R2 = H, aryloxy, arylmercapto, 1-5C alkyl or 1-3C hydroxyalkyl; or  
 R1+R2 = 3-5C alkylene;  
 R3 = H, 1-5C alkyl, benzyl, naphthyl or phenyl (optionally substituted by 1-3 of 1-5C alkyl, 1-5C alkoxy, 1-3C hydroxyalkyl, 2-5C alkoxy-carbonyl, 1-3C alkylmercapto, 1-4C alkylamino, 2-8C dialkylamino, halo, trifluoromethyl, COOH, CN, OH, nitro, amino, acetamido).  
 USE - The composition is used to suppress changes in the heart (e.g. reduced left ventricle function, enlargement of myocardial cells) associated with diabetes.  
 ADVANTAGE - Experiments were made with normal (OLETF) rats where diabetes had been induced, and diabetes-resistant rats (LETO).  
 Edaravone (test compound) or vehicle only (untreated) were administered orally twice daily for 2 weeks to the diabetic rats. The myocardial diameter of the cells (in microns) was 17.6 (normals), 19.9 (initial, diabetic), 23.1 (diabetic, untreated), 16.2 (treated).  
 Dwg.0/2  
 FS CPI  
 FA AB; GI; DCN  
 MC CPI: B07-D08; B14-F01; B14-F02  
 ABEX UPTX: 20031203  
 SPECIFIC COMPOUNDS - 70 Compounds are specifically claimed as (I) i.e.  
 (1) 3-methyl-1-phenyl-2-pyrazolin-5-one a.k.a. edaravone,  
 (2) 3-methyl-1-(2-methylphenyl)-2-pyrazolin-5-one,  
 (3) 3-methyl-1-(3-methylphenyl)-2-pyrazolin-5-one,  
 (4) 3-methyl-1-(4-methylphenyl)-2-pyrazolin-5-one,  
 (5) 3-methyl-1-(3,4-dimethylphenyl)-2-pyrazolin-5-one,

- (6) 1-(4-ethylphenyl)-3-methyl-2-pyrazolin-5-one,
- (7) 3-methyl-1-(4-propylphenyl)-2-pyrazolin-5-one,
- (8) 1-(4-butylphenyl)-3-methyl-2-pyrazolin-5-one,
- (9) 1-(3-trifluoromethylphenyl)-3-methyl-2-pyrazolin-5-one,
- (10) 1-(4-trifluoromethylphenyl)-3-methyl-2-pyrazolin-5-one,
- (11) 1-(2-methoxyphenyl)-3-methyl-2-pyrazolin-5-one,
- (12) 1-(3-methoxyphenyl)-3-methyl-2-pyrazolin-5-one,
- (13) 1-(4-methoxyphenyl)-3-methyl-2-pyrazolin-5-one,
- (14) 1-(3,4-dimethoxyphenyl)-3-methyl-2-pyrazolin-5-one,
- (15) 1-(4-ethoxyphenyl)-3-methyl-2-pyrazolin-5-one,
- (16) 3-methyl-1-(4-propoxyphenyl)-2-pyrazolin-5-one,
- (17) 1-(4-butoxyphenyl)-3-methyl-2-pyrazolin-5-one,
- (18) 1-(2-chlorophenyl)-3-methyl-2-pyrazolin-5-one,
- (19) 1-(3-chlorophenyl)-3-methyl-2-pyrazolin-5-one,
- (20) 1-(4-chlorophenyl)-3-methyl-2-pyrazolin-5-one,
- (21) 1-(3,4-dichlorophenyl)-3-methyl-2-pyrazolin-5-one,
- (22) 1-(4-bromophenyl)-3-methyl-2-pyrazolin-5-one,
- (23) 1-(4-fluorophenyl)-3-methyl-2-pyrazolin-5-one,
- (24) 1-(3-chloro-4-methylphenyl)-3-methyl-2-pyrazolin-5-one,
- (25) 1-(3-methylmercaptophenyl)-3-methyl-2-pyrazolin-5-one,
- (26) 1-(4-methylmercaptophenyl)-3-methyl-2-pyrazolin-5-one,
- (27) 4-(3-methyl-5-oxo-2-pyrazolin-1-yl) benzoic acid,
- (28) 1-(4-ethoxycarbonylphenyl)-3-methyl-2-pyrazolin-5-one,
- (29) 1-(4-nitrophenyl)-3-methyl-2-pyrazolin-5-one,
- (30) 3-ethyl-1-phenyl-2-pyrazolin-5-one,
- (31) 1-phenyl-3-propyl-2-pyrazolin-5-one,
- (32) 1,3-diphenyl-2-pyrazolin-5-one,
- (33) 3-phenyl-1-(p-tolyl)-2-pyrazolin-5-one,
- (34) 1-(4-methoxyphenyl)-3-methyl-2-pyrazolin-5-one,
- (35) 1-(4-chlorophenyl)-3-methyl-2-pyrazolin-5-one,
- (36) 3,4-diethyl-1-phenyl-2-pyrazolin-5-one,
- (37) 4-isobutyl-3-methyl-1-phenyl-2-pyrazolin-5-one,
- (38) 4-(2-hydroxyethyl)-3-methyl-1-phenyl-2-pyrazolin-5-one,
- (39) 3-methyl-4-phenoxy-1-phenyl-2-pyrazolin-5-one,
- (40) 3-methyl-4-phenylmercapto-1-phenyl-2-pyrazolin-5-one,
- (41) 2,3a,4,5,6,7-hexahydro-2-pyrazolin-5-one,
- (42) 3-(ethoxycarbonylmethyl)-1-phenyl-2-pyrazolin-5-one,
- (43) 1-phenyl-2-pyrazolin-5-one,
- (44) 3-methyl-2-pyrazolin-5-one,
- (45) 1,3-dimethyl-2-pyrazolin-5-one,
- (46) 1-ethyl-3-methyl-2-pyrazolin-5-one,
- (47) 1-butyl-3-methyl-2-pyrazolin-5-one,
- (48) 1-(2-hydroxyethyl)-3-methyl-2-pyrazolin-5-one,
- (49) 1-cyclohexyl-3-methyl-2-pyrazolin-5-one,
- (50) 1-benzyl-3-methyl-2-pyrazolin-5-one,
- (51) 1-(alpha-naphthyl)-3-methyl-2-pyrazolin-5-one,
- (52) 1-methyl-3-phenyl-2-pyrazolin-5-one,
- (53) 3-methyl-1-(4-methylphenyl)-2-pyrazolin-5-one,
- (54) 1-(4-butylphenyl)-3-methyl-2-pyrazolin-5-one,
- (55) 1-(4-methoxyphenyl)-3-methyl-2-pyrazolin-5-one,
- (56) 1-(4-butoxyphenyl)-3-methyl-2-pyrazolin-5-one,
- (57) 1-(4-chlorophenyl)-3-methyl-2-pyrazolin-5-one,
- (58) 1-(4-hydroxyphenyl)-3-methyl-2-pyrazolin-5-one,
- (59) 1-(3,4-dihydroxyphenyl)-3-methyl-2-pyrazolin-5-one,
- (60) 1-(2-hydroxyphenyl)-3-methyl-2-pyrazolin-5-one,
- (61) 1-(3-hydroxyphenyl)-3-methyl-2-pyrazolin-5-one,
- (62) 1-(4-hydroxyphenyl)-3-phenyl-2-pyrazolin-5-one,
- (63) 1-(4-hydroxymethylphenyl)-3-methyl-2-pyrazolin-5-one,

- (64) 1-(4-aminophenyl)-3-methyl-2-pyrazolin-5-one,  
 (65) 1-(4-methylaminophenyl)-3-methyl-2-pyrazolin-5-one,  
 (66) 1-(4-ethylaminophenyl)-3-methyl-2-pyrazolin-5-one,  
 (67) 1-(4-butylaminophenyl)-3-methyl-2-pyrazolin-5-one,  
 (68) 1-(3,4-dimethylaminophenyl)-3-methyl-2-pyrazolin-5-one,  
 (69) 1-(acetoamidophenyl)-3-methyl-2-pyrazolin-5-one,  
 (70) 1-(4-cyanophenyl)-3-methyl-2-pyrazolin-5-one.

ADMINISTRATION - 0.1-1000 (0.5-50) mg/kg orally or 0.01-100 (0.1-10) mg/kg by other routes.

L117 ANSWER 18 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2003-767492 [72] WPIX

DNC C2003-210946

TI Agents for treating and preventing hypoxic ischemic brain disorders comprise 2-pyrazolin-5-one derivative.

DC B03

IN IKEDA, T; IKENOUE, T

PA (MITS-N) MITSUBISHI PHARMA CORP

CYC 102

PI WO 2003078401 A1 20030925 (200372)\* JA 29 C07D231-20

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS

LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK

DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ

LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT

RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA

ZM ZW

AU 2003213364 A1 20030929 (200432) C07D231-20

ADT WO 2003078401 A1 WO 2003-JP3067 20030314; AU 2003213364 A1 AU 2003-213364 20030314

FDT AU 2003213364 A1 Based on WO 2003078401

PRAI JP 2002-71595 20020315

IC ICM C07D231-20

ICS A61K031-4152; A61P009-00; A61P025-00; A61P043-00; C07D231-22

AB WO2003078401 A UPAB: 20031107

NOVELTY - Agents for treating and preventing hypoxic ischemic brain disorders comprise a 2-pyrazolin-5-one derivative (I).

DETAILED DESCRIPTION - Agents for treating and preventing hypoxic ischemic brain disorders comprise a 2-pyrazolin-5-one derivative of formula (I) or its salt, hydrate or solvate.

R1 = H, aryl, Alk or 3-6C alkoxycarbonylalkyl; and

R2 = H, aryloxy, arylthio, Alk or 1-3C hydroxyalkyl; or

R1+R2 = 3-5C alkylene;

Alk = 1-5C alkyl; and

R3 = H, Alk, 5-7C cycloalkyl, 1-3C hydroxyalkyl, benzyl, naphthyl or phenyl (optionally substituted by 1-3 OAlk, 1-3C hydroxyalkyl, 2-5C alkoxycarbonyl, 1-3C alkylthio, 1-4C alkylamino, 2-8C dialkylaminohalo (sic), CF3, COOH, CN, OH, NO2, NH2 or acetamido).

ACTIVITY - Cerebroprotective; Vasotropic. In a hypoxic ischemia model on rats administration of edaravone at 6 mg/kg by tail vein injection significantly (p is less than 0.05) reduced cerebral nerve damage.

MECHANISM OF ACTION - Antioxidant.

USE - As free radical scavengers for treating and preventing hypoxic ischemic brain disorders especially due to labor in newborns.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B06-D05; B07-D08; B14-F02D1; B14-S08

ABEX

UPTX: 20031107

SPECIFIC COMPOUNDS - The use of about 30 compounds (I) is specifically claimed e.g. 1-phenyl-3-methyl-2-pyrazolin-5-one (Ia; edaravone).

ADMINISTRATION - Dosage is 0.01-100 (preferably 0.1-10) mg/kg/day by injection or 0.1-1000 (preferably 0.5-50) mg/kg/day orally.

L117 ANSWER 19 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2003-731523 [69] WPIX

DNC C2003-201348

TI New agents for preserving hearts for transplantation comprising pyrazolone derivative.

DC B03 D22 E13

IN FUKUMOTO, J; KITAMURA, N; YOSHIKAWA, T

PA (MITS-N) MITSUBISHI PHARMA CORP

CYC 102

PI WO 2003067979 A1 20030821 (200369)\* JA 42 A01N001-02

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS  
LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT  
RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA  
ZM ZW

AU 2003211983 A1 20030904 (200428) A01N001-02

JP 2003567178 X 20050602 (200537) 20 A01N001-02

ADT WO 2003067979 A1 WO 2003-JP1554 20030214; AU 2003211983 A1 AU 2003-211983 20030214; JP 2003567178 X JP 2003-567178 20030214, WO 2003-JP1554 20030214

FDT AU 2003211983 A1 Based on WO 2003067979; JP 2003567178 X Based on WO 2003067979

PRAI JP 2002-39354 20020215

IC ICM A01N001-02

ICS A61K031-4152; A61K031-41522; A61P009-10; A61P009-100; A61P041-00;  
A61P041-000; A61P043-00; A61P043-000

AB WO2003067979 A UPAB: 20031027

NOVELTY - An agent comprising a pyrazolone derivative (I) or its salt, is new.

DETAILED DESCRIPTION - An agent comprising a pyrazolone derivative of formula (I) or its salt, is new.

R1 = H, aryl, 1-5C alkyl or 3-6C cycloalkyl;

R2 = H, O-aryl, S-aryl, 1-5C alkyl or 1-3C hydroxyalkyl; or

R1+R2 = 3-5C alkylene; and

R3 = H, 1-5C alkyl, 5-7C cycloalkyl, 1-3C hydroxyalkyl, benzyl, naphthyl or phenyl (optionally substituted by 1-3 of 1-5C hydroxyalkyl, 1-3C hydroxyalkyl, 2-5C alkoxy carbonyl, 1-3C alkylthio, 1-4C alkylamino, 2-8C dialkylamino, halo, CF<sub>3</sub>, COOH, CN, OH, NO<sub>2</sub>, NH<sub>2</sub> or acetoamido).

An INDEPENDENT CLAIM is also included for an agent for preventing ischemic reperfusion injury after heart transplantation comprising (I).

ACTIVITY - Vasotropic.

Hearts removed from dogs and stored in a solution containing 15 mg/100 ml of 3-methyl-1-phenyl-

2-pyrazolin-5-one (Ia), reduced creatine phosphate kinase levels after 60 minutes to 77.8 ng/ml compared to 284.0 ng/ml for a control.

MECHANISM OF ACTION - None given in the source material.

USE - For preserving hearts and preventing ischemic reperfusion injury after heart transplantation.

ADVANTAGE - (I) Can be used without Euro-Collins solution.

Dwg.0/0



FS CPI  
 FA AB; GI; DCN  
 MC CPI: B07-D08; B14-F01B; B14-F01E; D09-A01C; E07-D08  
 TECH UPTX: 20031027  
 TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Agent: The agent is free of Euro-Collins solution.  
 ABEX UPTX: 20031027  
 SPECIFIC COMPOUNDS - The use of one compound (I) is specifically claimed, i.e. 3-methyl-1-phenyl-2-pyrazolin-5-one (Ia).  
 ADMINISTRATION - Dosage is 0.1 - 100 mg/kg by injection, nasally or orally.

L117 ANSWER 20 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN  
 AN 2003-720097 [68] WPIX  
 CR 1999-263624 [22]; 2003-585340 [55]; 2003-596829 [56]; 2003-730118 [69]; 2003-730119 [69]; 2003-743977 [70]; 2004-010082 [01]; 2004-041182 [04]; 2004-068835 [07]; 2004-339321 [31]; 2004-498809 [47]; 2004-498810 [47]; 2004-552334 [53]; 2004-552335 [53]; 2004-552336 [53]; 2004-552531 [53]; 2005-074026 [08]; 2005-080190 [09]; 2005-141329 [15]; 2005-151096 [16]; 2005-151097 [16]; 2005-151098 [16]; 2005-171345 [18]; 2005-171346 [18]  
 DNN N2003-575618 DNC C2003-198076  
 TI Propellant free buccal spray composition used for increasing rapid absorption of active compounds, comprises active compound such as antiarrhythmic, antihypertensive, heart regulator or vasodilator and polar solvent.  
 DC A96 B05 B07 P34  
 IN DUGGER, H A; DUGGER, H A I  
 PA (NOVA-N) NOVADEL PHARMA INC; (DUGG-I) DUGGER H A  
 CYC 106  
 PI US 2003077229 A1 20030424 (200368)\* 15 A61K009-00  
 WO 2004019909 A2 20040311 (200419) EN A61K009-12  
 RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS  
 LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW  
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
 KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH  
 PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VC VN  
 YU ZA ZM ZW  
 AU 2003270014 A1 20040319 (200462) A61K009-12  
 EP 1536769 A2 20050608 (200537) EN A61K009-12  
 R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV  
 MC MK NL PT RO SE SI SK TR  
 ADT US 2003077229 A1 CIP of WO 1997-US17899 19971001, CIP of US  
 2000-537118 20000329, US 2002-230075 20020829; WO  
 2004019909 A2 WO 2003-US26853 20030827; AU 2003270014 A1 AU 2003-270014  
 20030827; EP 1536769 A2 EP 2003-751909 20030827, WO 2003-US26853 20030827  
 FDT AU 2003270014 A1 Based on WO 2004019909; EP 1536769 A2 Based on WO  
 2004019909  
 PRAI US 2002-230075 20020829; WO 1997-US17899  
 19971001; US 2000-537118 20000329  
 IC ICM A61K009-00; A61K009-12  
 ICS A61K009-72; A61L009-04  
 AB US2003077229 A UPAB: 20050613  
 NOVELTY - Propellant free buccal spray composition comprises 0.001-60 weight% active compounds such as antiarrhythmics, antihypertensives, heart regulators, plaque stabilization agents, vasodilators, antianginals, anticoagulants, antihypotensives, antithrombotics, drugs for treating congestive heart failure and/or p-fox (fatty acid oxidation) inhibitors

and 30-99 weight% polar solvent.

DETAILED DESCRIPTION - Propellant free buccal spray composition comprises 0.001-60 weight% active compounds comprising antiarrhythmics, antihypertensives, heart regulators, cardiovascular agents, plaque stabilization agents, vasodilators, antianginals, anticoagulants, antihypotensives, antithrombotics, drugs for treating congestive heart failure and/or p-fox (fatty acid oxidation) inhibitors and 30-99 weight% polar solvent.

ACTIVITY - Antiarrhythmic; Hypotensive; Cardiovascular-Gen.; Vasodilator; Antianginal; Anticoagulant; Hypertensive. No biological data given.

MECHANISM OF ACTION - Fatty-Acid-Oxidation-Inhibitor.

USE - Used as a buccal aerosol spray or soft bite gelatin capsule for enhancing rapid absorption of active compounds through the oral mucosa.

Dwg. 0/0

FS CPI GMPI

FA AB; DCN

MC CPI: A12-V01; B01-B03; B01-C02; B01-C06; B01-D01; B04-B03A; B04-C01D; B04-C01G; B04-C02E; B04-C03C; B04-G01; B05-B01E; B06-H; B07-H; B10-A05; B10-A08; B10-A12C; B10-A17; B10-A22; B10-B01A; B10-B02E; B10-B02F; B10-B03B; B10-C04A; B10-E04D; B10-F02; B10-J02; B14-F01; B14-F02; B14-F04; B14-L06

TECH UPTX: 20031017

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Composition: The composition also comprises 0.1-10 (preferably 0.1-2.5) wt.% flavoring agent, 37-98 (preferably 25-97) wt.% or 0.05-10 wt.% polar solvent and 0.005-55 (preferably 0.2-25) wt.% active compound. The polar solvent comprises polyethylene glycols having a molecular weight of 400-1000, 2-8C mono- and poly-alcohols or 7-18C alcohols of linear or branched configuration, preferably aqueous polyethylene glycol or ethanol.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The antiarrhythmic agent comprises adenosine, amiodarone, bepridil, bretylium, digitoxin, digoxin, diltiazem, disopyramide, D-sotalol, flecainide, lidocaine, mexiletine, milrinone, phenytoin, pilsicainide, procainamide, propafenone, propranolol, quinidine, tocainide and/or dofetilide. The antihypertensive agent comprises acebutolol, alfuzosin, atenolol, amlodipine/benazepril, barnidipine, benazepril, bepridil, betaxolol, bisoprolol, bosentan, candesartan, captopril, cariporide, carvedilol, celiprolol, cilazapril, clonidine, diltiazem, doxazosin, enalapril, eplerenone, eprosartan, esmolol, felodipine, fenoldopam, fosinopril, guanfacine, imidapril, irbesartan, isradipine, labetalol, lercanidipine, lisinopril, losartan, maniidipine, methyldopa, metoprolol, moxonidine, nadolol, nicardipine, nicorandil, nifedipine, nitrendipine, nosoldipine, omapatrilat, perindopril, erbumine, pindolol, prazosin, propranolol, quinapril, ramipri, sotalol, spirapril, tamsulosin, telmisartan, terazosin, torsemide, trandolapril, valsartan, vatanidipine and/or midodrine.

The heart regulator comprises digoxin, digitoxin and/or dobutamine. The cardiovascular agent comprises edaravone, iloprost, levosimendan, molsidomine, tezosentan, tirilazad, YM087, adenosine, avasimibe and/or fenofibrate. The plaque stabilization agent comprises avasimibe.

The vasodilator comprises buflomedil, cilostazol, dipyridamole, diazoxide, hydralazine, minoxidil, naftidrofuryl, nicorandil, nitroprusside, alprostadil, apomorphine, phentolamine mesylate, sildenafil, tadalafil and/or vardenafil. The antianginal agent comprises amlodipine, amyl nitrite, atenolol, bepridil, diltiazem, erythrityl tetranitrate, felodipine, isosorbide dinitrate, isradipine, metoprolol, nadolol, nicardipine, nifedipine, nimodipine, pentaerythritol tetranitrate and/or propranolol. The anticoagulant comprises abciximab, ardeparin, argatroban,

bivalirudin, clopidogrel, dalteparin, danaparoid, desirudin, dipyridamole, enoxaparin, eptifibrate, fondaparinux, H376/95, lepirudin, melagatran, nadroparine, nafamostat, mesilate, pentosan, pentoxifylline, reviparin, sarpogrelatam SNAC/SNAD-heparin, ticlopidine, tinzaparin, tirofiban and/or warfarin. The antihypotensive agent comprises midodrine, dobutamine and/or fludrocortisone. The antithrombotic agent comprises aspirin, abciximab, enoxaparin, integrelin and/or ticlopidine. The drug for congestive heart failure comprises amrinone, benazepril, bumetanide, captopril, digitoxin, digoxin, dobutamide, dopamine, enalapril, ethacrynic acid, fosinopril, furosemide, hydralazine, lisinopril, milrinone, minoxidil, moexipril, quinapril, ramipril and/or torseamide. The p-FOX inhibitor comprises ranolazine.

The flavoring agent comprises synthetic or natural oil of peppermint, oil of spearmint, citrus oil, fruit flavors and/or sweeteners.

Alternatively, the composition contains 10-97 (preferably 20-97) wt.% polar solvent, 2-10 (preferably 2-4) wt.% propellant such as 3-8C hydrocarbon, 0.05-10 wt.% flavoring agent and 0.1-15 wt.% active compound. The propellant comprises propane, n-butane, isobutane, n-pentane, isopentane and/or neo-pentane.

ABEX UPTX: 20031017

ADMINISTRATION - Administration is by spraying on the oral mucosa. No dosage is given.

EXAMPLE - An antiemetic capsule was formulated by mixing (in weight%): dimenhydrinate (3-15), glycerin (10-12.5), polyethylene glycol (55-85) and flavors (3-6).

L117 ANSWER 21 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2003-663531 [62] WPIX

DNC C2003-180300

TI Agents for treating or preventing cardiac disorders, especially ischemic reperfusion disorders, comprise pyrazolone derivative.

DC B03

IN KITADA, Y; SATOH, N

PA (MITS-N) MITSUBISHI PHARMA CORP

CYC 102

PI WO 2003066051 A1 20030814 (200362)\* JA 29 A61K031-4152

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS  
LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT  
RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA  
ZM ZW

AU 2003207275 A1 20030902 (200425) A61K031-4152

JP 2003565475 X 20050526 (200535) 16 A61K031-4152

ADT WO 2003066051 A1 WO 2003-JP1229 20030206; AU 2003207275 A1 AU 2003-207275 20030206; JP 2003565475 X JP 2003-565475 20030206, WO 2003-JP1229 20030206

FDT AU 2003207275 A1 Based on WO 2003066051; JP 2003565475 X Based on WO 2003066051

PRAI JP 2002-30148 20020206

IC ICM A61K031-4152

ICS A61P009-00; A61P009-000; A61P009-04; A61P009-10; A61P009-100;  
C07D231-20; C07D231-26; C07D231-266

AB WO2003066051 A UPAB: 20030928

NOVELTY - Agents for treating or preventing cardiac disorders comprise a pyrazolone derivative (I).

DETAILED DESCRIPTION - Agents for treating or preventing cardiac disorders comprise a pyrazolone derivative of formula (I) or its salt or hydrate.

R1 = H, aryl, 1-5C alkyl or 3-6C alkoxy carbonylalkyl;  
 R2 = H, aryloxy, arylthio, 1-5C alkyl or 1-3 (sic) hydroxyalkyl; or  
 R1+R2 = 3-5C alkylene; and  
 R3 = H, 1-5C alkyl, 5-7C cycloalkyl, 1-3C hydroxyalkyl, benzyl, naphthyl or phenyl (optionally substituted by 1-3 1-5C alkoxy, 1-3C hydroxyalkyl, 2-5C alkoxy carbonyl, 1-3C alkylthio, 1-4C alkylamino, 2-8C dialkylamino, halo, CF<sub>3</sub>, COOH, CN, OH, NO<sub>2</sub>, NH<sub>2</sub> or acetamido).

ACTIVITY - Cardiant; Vasotropic.

In a myocardial ischemia model in dogs, 1-phenyl-3-methyl-2-pyrazol-5-one at 1 mg/kg/hr by i.v. administered within 10 minutes of ischemic event significantly (p is less than 0.05) improved left ventricular diastolic function compared to a control.

MECHANISM OF ACTION - None given.

USE - The agent is used for treating or preventing cardiac disorders especially ischemic reperfusion disorders such as reocclusion after percutaneous transluminal coronary angioplasty.

Dwg.0/2

FS CPI

FA AB; GI; DCN

MC CPI: B06-D05; B06-D07; B07-D08; B14-F02D; B14-F05

ABEX UPTX: 20030928

ADMINISTRATION - Dosage is 0.1-100 mg/kg by injection, orally or as eyedrops

L117 ANSWER 22 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2003-630052 [60] WPIX

DNC C2003-172451

TI New oxidation stress inhibitor, for treatment and/or prevention of oxidation stress, comprising pyrazolone derivative.

DC B03

PA (TANB) TT PHARM INC

CYC 1

PI JP 2003081830 A 20030319 (200360)\* 9 A61K031-4152

ADT JP 2003081830 A JP 2001-276623 20010912

PRAI JP 2001-276623 20010912

IC ICM A61K031-4152

ICS A61K031-416; A61P001-16; A61P003-10; A61P009-04;  
 A61P009-10; A61P009-14; A61P013-12; A61P017-16; A61P025-18;  
 A61P025-28; A61P027-06; A61P027-12; A61P035-00; A61P037-06

ICA C07D231-26

AB JP2003081830 A UPAB: 20030919

NOVELTY - New oxidation stress inhibitor comprises pyrazolone derivative or their salts as active ingredient.

DETAILED DESCRIPTION - New oxidation stress inhibitor comprises pyrazolone derivative of formula (I) or their salts as active ingredient.

R1 = H, aryl, 1-5C alkyl or 3-6C alkoxy carbonylalkyl;  
 R2 = H, aryloxy, arylmercapto, 1-5C alkyl or 1-3C hydroxyalkyl;  
 R1+R2 = 3-5C alkylene;  
 R3 = H, 1-5C alkyl, 5-7C cycloalkyl, 1-3C hydroxyalkyl, benzyl, naphthyl or optionally substituted phenyl.

ACTIVITY - Cerebroprotective; Vasotropic; Nootropic; Neuroprotective; Antilipemic.

MECHANISM OF ACTION - None given.

USE - The oxidation stress inhibitor is used for the treatment and/or prevention of oxidation stress disorder such as cerebrovascular disorder, vascular dementia, various peripheral circulatory disturbances, which are accompanied with an increase of monounsaturated fatty acid (claimed).

ADVANTAGE - The oxidation stress inhibitor inhibits oxidation stress by inhibiting monounsaturated fatty acid in a body (claimed).

Dwg.0/2

FS CPI  
 FA AB; GI; DCN  
 MC CPI: B06-D05; B06-D07; B07-D08; B14-F02; B14-F02F;  
 B14-F06

TECH UPTX: 20030919  
 TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Composition: 3-  
**Methyl-1-phenyl-2-pyrazolin**  
 -5-one or its salts are used as active ingredients.

ABEX UPTX: 20030919  
 DEFINITIONS - Preferred Definitions:  
 R1 = 1-5C alkyl;  
 R2 = H;  
 R3 = substituted phenyl.

L117 ANSWER 23 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2003-522788 [49] WPIX

CR 2005-384736 [39]

DNC C2003-140452

TI Treatment of animal with vascular senescence by administering to the  
 animal agent comprising premature vascular senescence ameliorating  
 ebselen-class compounds.

DC B05

IN CHEN, J; GOLIGORSKY, M S

PA (CHEN-I) CHEN; (GOLI-I) GOLIGORSKY M S

CYC 1

PI US 2003086916 A1 20030508 (200349)\* 11 A61K038-44

ADT US 2003086916 A1 Provisional US 2001-329010P 20011012, US  
 2002-269032 20021011

PRAI US 2001-329010P 20011012; US 2002-269032  
 20021011

IC ICM A61K038-44

ICS A61K031-192; A61K031-198; A61K031-353; A61K031-416; A61K031-445;  
 A61K031-555; A61K035-78

AB US2003086916 A UPAB: 20050621

NOVELTY - Treating vascular senescence involves administering an agent  
 comprising premature vascular senescence ameliorating ebselen-class  
 compounds.

ACTIVITY - Antidiabetic; Dermatological; Immunosuppressive;  
 Nootropic; Neuroprotective.

A thirty year old patient with type I diabetes mellitus, past medical  
 history of myocardial infarction, peripheral vascular disease,  
 hypertension, proteinuria, and non-healing foot ulcer, was receiving  
 insulin but experienced poor therapeutic response. Patient's fasting blood  
 glucose level was 200 mg/dl. The patient was given ebselen at 1-20 mg/kg,  
 3 times/day. After 6 months, the patient showed improvement of coronary  
 symptoms, healing of foot ulcer, normalization of blood pressure, and a  
 decrease in pentosidine ( at most 1.7 pmol/mg), and/or Amadori serum  
 albumin ( at most 30 U/ml).

MECHANISM OF ACTION - None given.

USE - The method is for treating an animal, preferably human, with  
 vascular senescence or elevated level of advanced glycation end products  
 in blood or tissue, e.g. end stage renal disease, chronic renal disease,  
 or peripheral vascular disease, poorly controlled diabetes, systemic lupus  
 erythematosus, Alzheimer's disease, or any neurodegenerative disease  
 (claimed).

ADVANTAGE - The method prevents the occurrence of premature  
 senescence in vascular tissue or cells by incubating the tissue or cells  
 with a premature vascular senescence preventing agent, and ameliorates  
 senescence of vascular endothelial cells in vitro or ex vivo by exposing  
 the cells to an ebselen-class compound.

Dwg.0/1  
 FS CPI  
 FA AB; DCN  
 MC CPI: B04-A06; B04-A08C; B04-A10H; B04-F01; B04-L03D; B05-A01B; B05-A03A;  
 B06-A01; B06-D09; B06-D18; B06-E05; B07-A02A; B07-D05; B07-D08;  
 B10-A20; B10-B01B; B10-C03; B10-E02; B11-C04A; B14-F02F;  
 B14-G02D; B14-J01A; B14-N10; B14-N17; B14-S04  
 TECH UPTX: 20030731  
 TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Method: The method also involves administering to the animal an agent consisting of premature vascular senescence ameliorating peroxynitrite formation inhibitors, that do not diminish nitric oxide synthesis or activity. It also involves treating the tissue or cells after seeding onto a substrate. Preferred Component: The substrate includes stent, artificial heart valve, artificial vascular graft, xenograft, or allograft.  
 TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Component: The agent comprising premature vascular senescence ameliorating ebselen-class compounds, comprises cysteine, cysteine and methionine substituted with tellurium or selenium, polyphenols, flavonoids, plant polyphenols, sinapic acid, 3,5-dimethoxy-4-hydroxycinnamic acid, quercetin, resorufin, bark extract containing hamamelitannin, phenolic acids, caffeic, chlorogenic and ferulic acids, uric acid, 3-methyl-1-phenyl-2-pyrazolin-5-one, 5,10,15,20-tetrakis(2,4,6-trimethyl-3,5-disulfonatophenyl)-porphyrinato iron (III), 5,10,15,20-tetrakis(N-methyl-4'-pyridyl)-porphyrinato iron (III), and 2,3,6-tribromo-4,5-dihydroxybenz methyl ether (TDB), or 2-phenyl-1,2-benziselenazol-3(2H)-one. The agent comprising premature vascular senescence ameliorating peroxynitrite formation inhibitors that do not diminish nitric oxide synthesis or activity, comprises manganese metalloporphyrins, (5,10,15,20-tetrakis(4-carboxyphenyl)-porphyrinato)manganese (III) chloride manganese (III) mesotetrakis (N-ethylpyridinium-2-yl)porphyrin, Mn(II) complex with a bis(cyclohexyl pyridine)-substituted macrocyclic ligand, salen-manganese complexes, CuZn-SOD that has been engineered to include positively charged glycine and arginine containing carboxy-terminal tail, hexamethylenediamine-conjugated SOD, SOD entrapped in cationic liposomes, pegalated SOD, or 4-hydroxytetramethylpiperidine-1-oxyl.  
 Preferred Method: The ebselen compound can be administered in mixture with antioxidant agents and vitamins with or without L-arginine or N-omega-hydroxy-L-arginine supplementation (20 mg/kg every 4 hours). The ebselen-class compounds may contain inert diluent and may be compressed into tablets, or may be formulated into elixir, suspension, or syrup. It may be impregnated into transdermal patches or may be contained in subcutaneous inserts.  
 ABEX UPTX: 20030731  
 ADMINISTRATION - Dosage comprises 0.01 micromol/kg to 2 mmol/kg; or 0.01-10 mg/kg, followed by 0.01-10 mg/kg/hour for peroxynitrite scavengers. Administration is transdermal, intravenous, intramuscular, or preferably oral.  
 L117 ANSWER 24 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN  
 AN 2003-498394 [47] WPIX  
 DNN N2003-396245 DNC C2003-133397  
 TI A method for correct quantitative determination of oxidative stress using a mono-unsaturated fatty acid as a marker.  
 DC B03 B04 S03  
 PA (TANB) TT PHARM INC  
 CYC 1  
 PI JP 2003083977 A 20030319 (200347)\* 11 G01N033-92  
 ADT JP 2003083977 A JP 2001-276622 20010912  
 PRAI JP 2001-276622 20010912

IC ICM G01N033-92  
ICS A61K031-4152; A61P001-16; A61P003-10; A61P009-10;  
A61P025-18; A61P035-00; G01N030-88; G01N033-50

ICA C07D231-22

AB JP2003083977 A UPAB: 20030723  
NOVELTY - A mono-unsaturated fatty acid as a marker for quantitative determination of oxidative stress.  
DETAILED DESCRIPTION - A method for quantitative determination of oxidative stress using a mono-unsaturated fatty acid, particularly oleic acid (18:1) and/or palmitoleic acid (16:1), in the living body as a marker, for diagnostic evaluation of pathogenic state of oxidative stress of patients with administered pyrazolone derivatives of formula (I).  
R1 = H, aryl, 1-5C alkyl, 3-6C alkoxy-carbonylalkyl;  
R2 = H, aryloxy, arylsulfhydryl, 1-5C alkyl, 1-3C hydroxyalkyl;  
R1 and R2 = 1-3C alkylene;  
R3 = H, 1-5C alkyl, 5-7C cycloalkyl, 1-3C hydroxyalkyl, benzyl or naphthyl, the phenyl is optionally substituted by 1-3 substituents selected from 1-5C alkyl, 1-5C alkoxy, 1-3C hydroxyalkyl, 2-5C alkoxy-carbonyl, 1-3C alkylsulfhydryl, 1-4C alkylamino, 2-8C dialkylamino, halo, trifluoromethyl, carboxyl, cyano, hydroxyl, nitro, amino or acetamide.  
USE - Determination of oxidative stress.  
ADVANTAGE - Determination of oxidative stress using blood without tissue invasion.  
Dwg.0/2

FS CPI EPI  
FA AB; GI; DCN  
MC CPI: B07-D08; B10-C04E; B11-C08; B12-K04A  
EPI: S03-E14H1

ABEX UPTX: 20030723  
SPECIFIC COMPOUNDS - 3-Methyl-1-phenyl-2-pyrazolin-5-one  
(Ia) is claimed as (I) and 72 compounds of (I) are disclosed.

EXAMPLE - The following steps were carried out:  
(1) preparation of middle cerebral artery (MCA) obstructed and re-perfused model rat,  
(2) administration of 3-methyl-1-phenyl-2-pyrazolin-5-one,  
(3) blood sampling and  
(4) isolation and determination of free fatty acids.

L117 ANSWER 25 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN  
AN 2003-342611 [32] WPIX  
DNN N2003-274051 DNC C2003-089980  
TI Composition for treating oxidative stress including e.g. ischemic conditions cerebrovascular disorders, cerebral embolism, stroke, vascular dementia, heart disease or myocardial infarct comprises 5-oxo-pyrazoline or its derivative.  
DC B03 S03  
IN TAKAHASHI, C; WATANABE, K; YAMAMOTO, Y  
PA (MITS-N) MITSUBISHI PHARMA CORP  
CYC 100  
PI WO 2003024446 A1 20030327 (200332)\* JA 44 A61K031-4152  
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU  
MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW  
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ  
LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO  
RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM

ZW

AU 2002330493 A1 20030401 (200452) A61K031-4152

JP 2003528542 X 20041224 (200502) A61K031-4152

ADT WO 2003024446 A1 WO 2002-JP9087 20020906; AU 2002330493 A1

AU 2002-330493 20020906; JP 2003528542 X WO 2002-JP9087

20020906, JP 2003-528542 20020906

FDT AU 2002330493 A1 Based on WO 2003024446; JP 2003528542 X Based on WO 2003024446

PRAI JP 2001-275467 20010911; JP 2001-275466

20010911

IC ICM A61K031-4152

ICS A61P001-16; A61P003-06; A61P003-10; A61P007-04;

A61P009-00; A61P009-10; A61P039-06; A61P043-00; C07D231-26;

G01N033-48; G01N033-92

AB WO2003024446 A UPAB: 20030522

NOVELTY - Composition for treating oxidative stress comprises 5-oxo-pyrazoline or its derivative (I).

DETAILED DESCRIPTION - Composition for treating oxidative stress comprises 5-oxo-pyrazoline or its derivatives of formula (I), or their salts, hydrates and solvates.

R1 = H, aryl, 1-5C alkyl or saturated 3-6C alkoxycarbonylalkyl;

R2 = H, aryloxy, aryl mercapto, 1-5C alkyl or 1-3C hydroxyalkyl; or

R1+R2 = 3-5C alkylene;

R3 = H, aryl, 1-5C alkyl, 5-7C cycloalkyl, 1-3C hydroxyalkyl, benzyl, naphthyl, or phenyl (optionally mono- to tri-substituted, by 1-5C alkyl, 1-5C alkoxy, 1-3C hydroxyalkyl, 2-5C alkoxycarbonyl, 1-3C alkylmercapto, 1-4C alkylamino, 2-8C dialkylamino, halo, trifluoromethyl, COOH, CN, OH, NO2, NH2, acetamido).

INDEPENDENT CLAIMS are also included for:

(1) measuring oxidative stress using monounsaturated fatty acid, ubiquinone-10 or cholesterol ester peroxide in blood plasma as a marker; and

(2) evaluating the treatment of oxidative stress.

ACTIVITY - Tranquillizer; Cerebroprotective; Cardiant; Hepatotropic; Antiinflammatory; Virucide; Ophthalmological; Antibacterial; Immunosuppressive.

No relevant biological data is given.

MECHANISM OF ACTION - None given.

USE - (I) is useful for treating oxidative stress conditions, e.g. ischemic conditions; including cerebrovascular disorders such as cerebral embolism and stroke, and other cerebral conditions such as reduction of cerebral function, vascular dementia, and age-related cerebrovascular tissue lesion, and heart disease such as myocardial infarct and heart failure, and peripheral circulation disorders; liver damage including alcoholic hepatitis; diabetes; retinal disease; glaucoma; side effects of radiotherapy; cerebral edema; endotoxic shock; nephritis.

ADVANTAGE - Measurements of oxidative stress can be made quantitatively and accurately.

Dwg.0/4

FS CPI EPI

FA AB; GI; DCN

MC CPI: B01-D02; B04-B01B; B04-B04D4; B06-D07; B07-D08; B10-A06; B11-C08; B12-K04A; B14-C03; B14-F01B; B14-F02D; B14-F02F3; B14-J01A4; B14-N03; B14-N10; B14-N12; B14-N16; B14-S04; B14-S08

EPI: S03-E14H

ABEX UPTX: 20030522

SPECIFIC COMPOUNDS - Use of 1 compound (I) is specifically claimed, i.e. 3-methyl-1-phenyl-2-pyrazolin-5-one ('Edaravone').



ADMINISTRATION - 0.01-100 (0.1-10) mg/kg non-orally (injection or drops) or 0.1-1000 (0.5-50) mg/kg orally for (I), and dosage in the same range for the anti-thrombus agent.

L117 ANSWER 26 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN  
 AN 2003-342610 [32] WPIX  
 DNC C2003-089979  
 TI Composition useful for treating ischemic conditions such as cerebrovascular disorders, age-related cerebrovascular tissue lesion, heart disease or myocardial infarct comprises anti-thrombus agent and pyrazolin-5-one or derivative.  
 DC B02 B03  
 IN EGUCHI, J; KURITA, K; TANAKA, M; TANAKA, T; YAMADA, K; YOSHII, N; YUKI, S  
 PA (MITS-N) MITSUBISHI PHARMA CORP; (EGUC-I) EGUCHI J; (KURI-I) KURITA K; (TANA-I) TANAKA M; (TANA-I) TANAKA T; (YAMA-I) YAMADA K; (YOSH-I) YOSHII N; (YUKI-I) YUKI S  
 CYC 101  
 PI WO 2003024445 A1 20030327 (200332)\* JA 26 A61K031-415  
 RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW  
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW  
 EP 1437137 A1 20040714 (200446) EN A61K031-415  
 R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR  
 AU 2002328553 A1 20030401 (200452) A61K031-415  
 KR 2004044514 A 20040528 (200463) A61K031-4152  
 JP 2003528541 X 20041224 (200502) A61K031-4152  
 US 2005009896 A1 20050113 (200506) A61K031-727  
 CN 1555261 A 20041215 (200519) A61K031-415  
 ADT WO 2003024445 A1 WO 2002-JP9425 20020913; EP 1437137 A1 EP 2002-760833 20020913, WO 2002-JP9425 20020913; AU 2002328553 A1 AU 2002-328553 20020913; KR 2004044514 A KR 2004-703013 20040227; JP 2003528541 X WO 2002-JP9425 20020913, JP 2003-528541 20020913; US 2005009896 A1 WO 2002-JP9425 20020913, US 2004-489507 20040903; CN 1555261 A CN 2002-817992 20020913  
 FDT EP 1437137 A1 Based on WO 2003024445; AU 2002328553 A1 Based on WO 2003024445; JP 2003528541 X Based on WO 2003024445  
 PRAI JP 2001-365032 20011129; JP 2001-279645 20010914  
 IC ICM A61K031-415; A61K031-4152; A61K031-727  
 ICS A61K031-4174; A61K031-4709; A61K031-557; A61K031-60; A61K045-00; A61P009-10; A61P043-00  
 ICA C07D231-22; C07D231-26; C07D231-28; C07D231-56  
 ICI C07D231-26, C07D231:22, C07D231:28, C07D231:56  
 AB WO2003024445 A UPAB: 20030522  
 NOVELTY - Composition for treating ischemic conditions comprises anti-thrombus agent (II) and pyrazolin-5-one or derivative  
 DETAILED DESCRIPTION - Composition contains an anti-thrombus agent (II) and pyrazolin-5-one or its derivatives of formula (I), or their salts, hydrates and solvates.  
 R1 = H, aryl, 1-5C alkyl or saturated 3-6C alkoxycarbonylalkyl;  
 R2 = H, aryloxy, aryl mercapto, 1-5C alkyl or 1-3C hydroxyalkyl; or R1+R2 = 3-5C alkylene;  
 R3 = H, aryl, 1-5C alkyl, 5-7C cycloalkyl, 1-3C hydroxyalkyl, benzyl,

naphthyl, or phenyl (optionally mono- to tri-substituted, by 1-5C alkyl, 1-5C alkoxy, 1-3C hydroxyalkyl, 2-5C alkoxy carbonyl, 1-3C alkylmercapto, 1-4C alkylamino, 2-8C dialkylamino, halo, trifluoromethyl, COOH, CN, OH, NO<sub>2</sub>, NH<sub>2</sub>, acetamido).

ACTIVITY - Cerebroprotective; Cardiant; Thrombolytic.

Edaravone (80 mg in isotonic solution) and/or Ozagrel sodium or Argatroban (80 mg in isotonic solution) was given intravenously, twice daily for 14 days, to patients with a diagnosis of cerebral embolism. The patients were assessed one month after the start of treatment and assigned a Modified Rankin Score of between 0 (no disease) and 6 (dead). 20 patients were given combined therapy (and 17 patients given anti-thrombus drugs only). The numbers with the specified scores for combined treatment (with numbers for anti-thrombus drugs only in brackets) as follows: score 0; 11 (6): score 1; 2 (3): score 2; 2 (3): score 3; 1 (2): score 4; 1 (0): score 5; 2 (3): score 6; 1 (0).

MECHANISM OF ACTION - Platelet Aggregation Inhibitor; Thromboxane Synthase Inhibitor.

USE - The composition is useful for treating ischemic conditions (claimed), including cerebrovascular disorders such as cerebral embolism and stroke; other cerebral conditions such as reduction of cerebral function, vascular dementia, age-related cerebrovascular tissue lesion; heart disease such as myocardial infarct, heart failure; and peripheral circulation disorders.

ADVANTAGE - The composition increases the effectiveness of the treatment, and reduces side-effects.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B06-D02; B06-D07; B07-D08; B07-D09; B14-D10; **B14-F01B**; **B14-F02D**; **B14-F02F3**; **B14-F04**; B14-J01A4; B14-L06; B14-N16

TECH UPTX: 20030522

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Agents: (II) is a thrombolytic, anticoagulant or platelet aggregation inhibitor, especially an anti-thrombin, a thromboxane synthase inhibitor or a tissue plasminogen activation factor.

ABEX UPTX: 20030522

SPECIFIC COMPOUNDS - Use of 1 compound (I) is specifically claimed, i.e. 3-methyl-1-phenyl-2-pyrazoline-5-one (Edaravone).

Use of 2 compounds (II) is specifically claimed, i.e.

(2R,4R)-4-methyl-1-(N2((RS)-3-methyl-1,2,3,4-tetrahydro-8-quinolin-sulfonyl)-L-arginylyl)-2-piperidinecarboxylic acid monohydrate (Argatroban) and/or sodium (E)-3-(p-(1H-imidazol-1-methyl)phenyl)-2-propenoate (Ozagrel sodium).

ADMINISTRATION - Administration is 0.01-100 (0.1-10) mg/kg non-orally (injection or drops) or 0.1-1000 (0.5-50) mg/kg orally for (I), and dosage in the same range for the anti-thrombus agent.

L117 ANSWER 27 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2003-120603 [11] WPIX

DNC C2003-031182

TI New injection preparation comprises a pyrazolone derivative in specific concentration range, useful for treating and preventing cerebral vascular disorders such as cerebral ischemia, cerebral apoplexy and cerebral edema.

DC B03

IN CHIBA, M; MATSUO, N; YOSHIDA, H

PA (MITS-N) MITSUBISHI PHARMA CORP; (CHIB-I) CHIBA M; (MATS-I) MATSUO N; (YOSH-I) YOSHIDA H

CYC 101

PI WO 2002092082 A1 20021121 (200311)\* JA 18 A61K031-4152 <--  
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
 NL OA PT SD SE SL SZ TR TZ UG ZM ZW  
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
 KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT  
 RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM  
 ZW

EP 1386606 A1 20040204 (200410) EN A61K031-4152  
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
 RO SE SI TR

KR 2003096377 A 20031224 (200426) A61K009-08  
 AU 2002255326 A1 20021125 (200452) A61K031-4152 <--  
 US 2004162330 A1 20040819 (200455) A61K031-4152  
 JP 2002588999 X 20040826 (200456) A61K031-4152  
 CN 1525856 A 20040901 (200478) A61K031-4152

ADT WO 2002092082 A1 WO 2002-JP4508 20020509; EP 1386606 A1 EP  
 2002-724736 20020509; WO 2002-JP4508 20020509; KR  
 2003096377 A KR 2003-714622 20031110; AU 2002255326 A1 AU 2002-255326  
 20020509; US 2004162330 A1 WO 2002-JP4508 20020509, US  
 2003-477275 20031211; JP 2002588999 X JP 2002-588999 20020509,  
 WO 2002-JP4508 20020509; CN 1525856 A CN 2002-809723  
 20020509

FDT EP 1386606 A1 Based on WO 2002092082; AU 2002255326 A1 Based on WO  
 2002092082; JP 2002588999 X Based on WO 2002092082

PRAI JP 2001-141683 20010511

IC ICM A61K009-08; A61K031-4152  
 ICS A61K047-10; A61K047-18; A61P009-00; A61P009-10

ICA C07D231-20

ICI C07D231:20

AB WO 200292082 A UPAB: 20030214

NOVELTY - New injection preparation comprises a pyrazolone derivative (I)  
 in an amount of 3-60 mg/ml.

DETAILED DESCRIPTION - New injection preparation comprises a  
 pyrazolone derivative of formula (I) or its salt, hydrate and/or solvate  
 in an amount of 3-60 mg/ml.

R1 = H, aryl, 1-5C alkyl or 3-6C alkoxy-carbonylalkyl;  
 R2 = H, aryloxy, arylthio, 1-5C alkyl or 1-3 hydroxyalkyl; or  
 R1+R2 = 3-5C alkylene;  
 R3 = H, 1-5C alkyl, 5-7C cycloalkyl, 1-3 hydroxyalkyl, benzyl,  
 naphthyl or phenyl (optionally substituted by 1-5C alkoxy, 1-3C  
 hydroxyalkyl, 2-5C alkoxy-carbonyl, 1-3C alkylthio, 1-4C alkylamino, 2-8C  
 dialkylamino, halo, CF3, COOH, CN, OH, NO2, NH2 or acetylamino).

USE - (I) are used as injection preparations for administering  
 pyrazolone derivatives such as edaravon (claimed) useful for  
 treating and preventing cerebral vascular disorders such as cerebral  
 ischemia, cerebral apoplexy and cerebral edema.

ADVANTAGE - (I) have high concentration and good long term stability,  
 e.g. on storage.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B06-D05; B06-D07; B07-D08; B14-F02D1; B14-N16

TECH UPTX: 20030214

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Preparation: Injection  
 preparation has a pH of 2.0-6.5 (preferably 3.0-4.5) and comprises 10-70  
 v/v% ethanol and 0.01-1 mg/ml stabilizer (preferably ethylenediamine,  
 disodium calcium edate or disodium edate).

ABEX UPTX: 20030214

SPECIFIC COMPOUNDS - The use of one compound (I) is specifically claimed, e.g. 3-methyl-1-phenyl-2-pyrazolin-5-one (edaravon).

EXAMPLE - An injection preparation comprised edaravon (1 g), ethanol (60 ml), disodium edate (20 mg), citric acid monohydrate (420 mg), trisodium citrate (294 mg), 1 mol/L hydrochloric acid (to pH 3.6) and water for injection (to 200 ml). In stability tests at 60 degreesC for 1 month % activity lost was 1.22%.

L117 ANSWER 28 OF 28 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN  
 AN 2002-139866 [18] WPIX  
 DNC C2002-043089  
 TI Agent useful for treating optic nerve disease comprises hydroxy radical scavenger.  
 DC B05  
 IN INOUE, E; MANO, T; SOGOU, S  
 PA (MITS-N) MITSUBISHI-TOKYO PHARM INC; (MITS-N) MITSUBISHI PHARMA CORP;  
 (INOUE-I) INOUE E; (MANO-I) MANO T; (SOGO-I) SOGOU S  
 CYC 95  
 PI WO 2002000260 A1 20020103 (200218)\* JA 15 A61K045-00 <--  
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
 NL OA PT SD SE SL SZ TR TZ UG ZW  
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM  
 DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC  
 LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE  
 SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW  
 AU 2001067864 A 20020108 (200235) A61K045-00 <--  
 EP 1297849 A1 20030402 (200325) EN A61K045-00  
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
 RO SE SI TR  
 US 2003109566 A1 20030612 (200340) A61K031-4152  
 JP 2002505041 X 20040108 (200406) A61K045-00  
 ADT WO 2002000260 A1 WO 2001-JP5585 20010628; AU 2001067864 A  
 AU 2001-67864 20010628; EP 1297849 A1 EP 2001-945674  
 20010628, WO 2001-JP5585 20010628; US 2003109566 A1 WO  
 2001-JP5585 20010628, US 2002-312502 20021227; JP  
 2002505041 X WO 2001-JP5585 20010628, JP 2002-505041  
 20010628  
 FDT AU 2001067864 A Based on WO 2002000260; EP 1297849 A1 Based on WO  
 2002000260; JP 2002505041 X Based on WO 2002000260  
 PRAI JP 2000-197250 20000629  
 IC ICM A61K031-4152; A61K045-00  
 ICS A61K009-06; A61K009-08; A61P025-02; A61P027-02; A61P039-06;  
 C07D231-26  
 AB WO 200200260 A UPAB: 20020319  
 NOVELTY - Agent for treating or preventing optic nerve disease comprises a  
 hydroxy radical scavenger.  
 DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the  
 use of a hydroxy radical scavenger comprising for treating and preventing  
 (a) retinal circulation disturbances such as retinal arterial obliteration  
 and retinal phlebemphraxis, (b) retinal disorders e.g. due to viral or  
 bacterial infections or iridocyclic disorders, (c) macular disorders,  
 degenerative disorders such as retinal pigment degeneration (d) retinal  
 peeling or (e) retinal disorders due to phenothiazine toxicity.  
 ACTIVITY - Ophthalmolgical; Virucide; Antibacterial; Antidote;  
 Antiinflammatory; Vasotropic; Cytostatic; Antialcohol.  
 In Wistar rats MCI-186 at 3 mg/kg significantly  
 (p is less than 0.01) reduced retinal degeneration due to transient  
 retinal ischemia.

## MECHANISM OF ACTION - Antioxidant

USE - As a hydroxy radical scavenger for treating and preventing optic nerve disease (e.g. due to inflammation, circulation disturbances such as ischemia, age related tumors, edema or alcohol poisoning), retinal circulation disturbances (such as retinal arterial obliteration and retinal phlebemphraxis), retinal disorders (e.g. due to viral or bacterial infections or iridocyclic disorders), macular disorders, degenerative disorders (such as retinal pigment degeneration), retinal peeling and retinal disorders due to phenothiazine toxicity.

Dwg.0/1

FS CPI

FA AB; DCN

MC CPI: B07-D08; B14-A01; B14-A02; B14-C03; **B14-F02D**; B14-H01;  
B14-M01A; B14-N03; B14-S08

=&gt; =&gt; d all l101

L101 ANSWER 1 OF 1 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

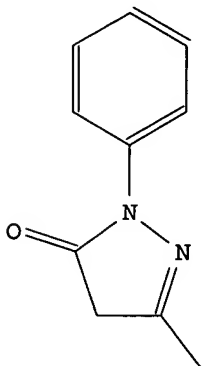
AN.S DCR-62787

DCSE 62787-0-0-0

CN.P EDARAVONE

CN.S 5-Methyl-2-phenyl-2,4-dihydro-pyrazol-3-one

SY 1-PHENYL-3-METHYL PYRAZOL-5-ONE; 3-METHYL-1-PHENYL-2-PYRAZOLIN-5-ONE;  
EDARAVONE; **MCI-186**; METHYL-1-PHENYL-2-PYRAZOLIN-5-ONE, 3-;  
NORPHENAZONE; PHENYL-3-METHYL PYRAZOL-5-ONE, 1-



MF C10 H10 N2 O

SMF C10 H10 N2 O \*1; TOTAL \*1; TYPE \*1

MW 174.202

SDCN R03069; R15061

=&gt; d his

(FILE 'HOME' ENTERED AT 09:38:26 ON 05 JUL 2005)

SET COST OFF

FILE 'HCAPLUS' ENTERED AT 09:38:42 ON 05 JUL 2005

L1 1 S US20040254234/PN OR (US2003-643404# OR JP2002-258503)/AP,PRN  
E TANAKA T/AU  
L2 1839 S E3-E9,E103  
E TAKAYUKI/AU  
L3 2 S E3

jan delaval - 5 july 2005

L4           1572 S E3-E7  
               E MORI T/AU  
 L5           15 S E7,E8  
               E MORI TATSU/AU  
               E TATSUHIKO M/AU  
               E MITSUBISHI/PA,CS  
 L6           136872 S MITSUBISHI?/PA,CS  
               SEL RN L1

FILE 'REGISTRY' ENTERED AT 09:41:24 ON 05 JUL 2005

L7           3 S E1-E3  
 L8           1 S L7 AND N2C3/ES  
 L9           21 S 89-25-8/CRN  
 L10          STR  
 L11          50 S L10  
 L12          93380 S L10 FUL  
 L13          STR L10  
 L14          50 S L13 CSS SAM SUB=L12  
 L15          STR L13  
 L16          39 S L15 CSS SAM SUB=L12  
 L17          2711 S L15 CSS FUL SUB=L12  
               SAV L17 KWON643/A  
 L18          STR L15  
 L19          0 S L18 CSS SAM SUB=L12  
 L20          6 S L18 CSS FUL SUB=L12  
               SAV L20 KWON643A/A  
 L21          STR L15  
 L22          22 S L21 CSS SAM SUB=L17  
 L23          472 S L21 CSS FUL SUB=L17  
               SAV L23 KWON643B/A  
 L24          STR L21  
 L25          27 S L24 CSS SAM SUB=L17  
 L26          480 S L24 CSS FUL SUB=L17  
               SAV L26 KWON643C/A  
 L27          5 S L20 NOT 748176-18-3  
 L28          957 S L23,L26,L27  
               SAV L28 KWON643D/A  
 L29          935 S L28 NOT L8,L9  
 L30          909 S L29 NOT (MXS OR PMS OR IDS)/CI  
 L31          44 S L30 AND NC>=2  
 L32          19 S L31 AND CLH AND 2/NC  
 L33          865 S L30 NOT L31  
 L34          884 S L32,L33

FILE 'HCAPLUS' ENTERED AT 10:05:39 ON 05 JUL 2005

L35          2230 S L8  
 L36          12 S L9  
 L37          2 S L36 AND (PHARMACEUT? OR PHARMACOL?)/SC,SX  
 L38          113 S EDARA!ON#  
 L39          86 S 1 PHENYL 3 METHYLPYRAZOL 5 ONE  
 L40          451 S 3 METHYL 1 PHENYL 2 PYRAZOLIN 5 ONE  
 L41          1585 S 1 PHENYL 3 METHYL 5 PYRAZOLONE  
 L42          552 S 3 METHYL 1 PHENYL 5 PYRAZOLONE  
 L43          138 S 1 PHENYL 3 METHYLPYRAZOLONE  
 L44          46 S 2 4 DIHYDRO 5 METHYL 2 PHENYL 3H PYRAZOL 3 ONE  
 L45          71 S MCI186 OR MCI 186  
 L46          177 S NORANTIPYRIN?  
 L47          36 S 3 METHYL 1 PHENYL 2 PYRAZOLINE 5 ONE  
 L48          21 S 1 PHENYL 3 METHYL 5 PYRAZOLINONE  
 L49          54 S 3 METHYL 1 PHENYLPYRAZOL 5 ONE

L50 2 S 3 METHYL 1 PHENYL 4 5 DIHYDROPYRAZOL 5 ONE  
 L51 4070 S L35-L50  
 L52 2338 S L34  
 L53 5809 S L51,L52  
 L54 114 S L53 AND L1-L6  
 L55 253 S ARTERIAL (L) WALL (L) FAIL?  
 L56 749 S ARTERIAL (L) WALL (L) INJUR?  
 L57 375 S ARTERIAL (L) WALL (L) DAMAG?  
 L58 1 S L53 AND L55-L57  
 E ARTERY, DISEASE/CT  
 E E3+ALL  
 L59 21055 S E7+OLD  
 L60 58106 S E7+NT  
 L61 76585 S E7+RT  
 E E54+ALL  
 L62 80239 S E5+OLD,NT  
 L63 23 S L53 AND L59-L62  
 L64 23 S L58,L63  
 L65 897 S PERCUTAN? (L) TRANSLUMIN? (L) (HEART OR MYOCARD? OR CORON?) (L) ANG  
 L66 913 S PTCA  
 L67 1193 S CORONAR? (L) ARTER? (L) BYPASS? (L) ?GRAFT?  
 L68 12 S CORONAR? (L) ARTER? (L) BY PASS? (L) ?GRAFT?  
 L69 472 S CABG  
 L70 1 S L53 AND L65-L69  
 E RESTENOSIS/CT  
 E E3+ALL  
 L71 4523 S E2,E3  
 L72 6548 S RESTENOS?  
 L73 2544 S NEOINTIM?  
 L74 3 S L53 AND L71-L73  
 L75 23 S L64,L70,L74  
 E BYPASS/CT  
 E CORONARY BYPASS/CT  
 L76 1 S E23  
 E ARTERIAL BYPASS/CT  
 L77 0 S L53 AND L76  
 L78 2 S L75 AND L54  
 L79 21 S L75 NOT L78  
 L80 11 S L79 AND (PD<=20020904 OR PRD<=20020904 OR AD<=20020904)  
 SEL DN AN 2 3 4 6 8  
 L81 5 S L80 AND E1-E15  
 L82 6 S L80 NOT L81  
 SEL DN AN 1 5  
 L83 2 S L82 AND E16-E21  
 L84 9 S L78,L81,L83  
 L85 9 S L84 AND L1-L6,L35-L84

FILE 'REGISTRY' ENTERED AT 10:37:20 ON 05 JUL 2005

FILE 'HCAPLUS' ENTERED AT 10:37:53 ON 05 JUL 2005

FILE 'MEDLINE' ENTERED AT 10:38:23 ON 05 JUL 2005

L86 3 S L34  
 L87 159 S L8 OR L9  
 L88 298 S L38-L50  
 L89 326 S L86-L88  
 L90 24 S L89 AND A7./CT  
 L91 69 S L89 AND C14./CT  
 L92 10 S L89 AND E4./CT  
 L93 7 S L90,L91 AND L92

E RESTENOSIS/CT  
E E4+ALL  
E E2+ALL  
L94 0 S L89 AND E9+NT  
L95 36 S L90-L93 AND PY<=2002  
L96 2 S L95 AND L93  
L97 11 S L90 AND L95  
L98 21 S L91 AND L95 NOT L93,L96,L97  
  
FILE 'WPIX' ENTERED AT 10:46:53 ON 05 JUL 2005  
L99 35 S L38/BI,ABEX  
L100 205 S L39/BI,ABEX OR L40/BI,ABEX OR L41/BI,ABEX OR L42/BI,ABEX OR L  
E MCI 186/DCN  
E MCI-186/DCN  
E MCI-186/CN  
L101 1 S E3  
L102 108 S R03069/DCN OR R15061/DCN  
L103 246 S L99,L100,L102  
L104 6 S L103 AND A61P003/IPC  
L105 29 S L103 AND P52?/M0,M1,M2,M3,M4,M5,M6  
L106 12 S L103 AND (B12-F01? OR C12-F01? OR B14-F01? OR C14-F01?)/MC  
L107 32 S L103 AND (B12-F? OR C12-F? OR B14-F? OR C14-F?)/MC  
L108 34 S L104-L107  
L109 2 S L103 AND (TANAKA T? OR MORI T? OR TAKAYUKI T? OR TATSUHIKO M?  
L110 28 S L103 AND MITSUBISHI?/PA  
L111 1 S L1  
L112 1 S L111 AND L103-L110  
L113 33 S L108 NOT L112  
L114 2 S L113 AND PY<=2002  
L115 27 S L113 AND PRY<=2002  
L116 16 S L113 AND AY<=2002  
L117 28 S L112,L114-L116

FILE 'WPIX' ENTERED AT 11:13:43 ON 05 JUL 2005

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